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EDUCATION:

Post Graduate Education:
M.D.
Michigan State University
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Undergraduate Education:
B.S. Biochemistry
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TRAINING:

7/97 – 6/98 Mammography, CT and Ultrasound Fellowship
Henry Ford Hospital, Detroit, Michigan
- Mammography: Experienced in Stereotactic Vacuum Assisted Core biopsies, Ultrasound Core biopsies/aspirations
- Computed Tomography: Experienced in percutaneous drainage, aspirations and biopsies
- Ultrasound: Skilled in abdominal, prostate, gynecologic and obstetric imaging

7/93 – 6/97 Diagnostic Radiology
St. Joseph Mercy Hospital, Oakland

9/94 – 1/95 Pediatric Radiology
Children's Hospital of Michigan

8/95 – 10/95 Armed Forces Institute of Pathology
Washington D.C.

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Providence Hospital
Southfield, Michigan

1/04 - Present Director of Mammography
St John/Providence Hospital System
Novi, Farmington, Livonia and Southfield, MI Locations

Exhibit A

LICENSURE: Permanent Medical License – Michigan (4301061906)
Diplomat, National Board of Medical Examiners
American Board of Radiology, Board Eligible

ORGANIZATION & ACTIVITIES:

American Roentgen Ray Society
American College of Radiology
Michigan State Medical Society
Society of Breast Imaging

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(54) BIOPSY DEVICES AND METHODS

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(57) ABSTRACT

An improved system for mammography analysis and methods of using the same. In one aspect, a clip comprises a first portion and at least one additional second portion connected to the first portion, the first and second portions adapted for elastic deformation for engaging tissue. In anther aspect, an improved actuator for performing a breast biopsy is used to deploy a clip. In yet another aspect of the invention, there is contemplated a system for marking an evacuated breast cyst.

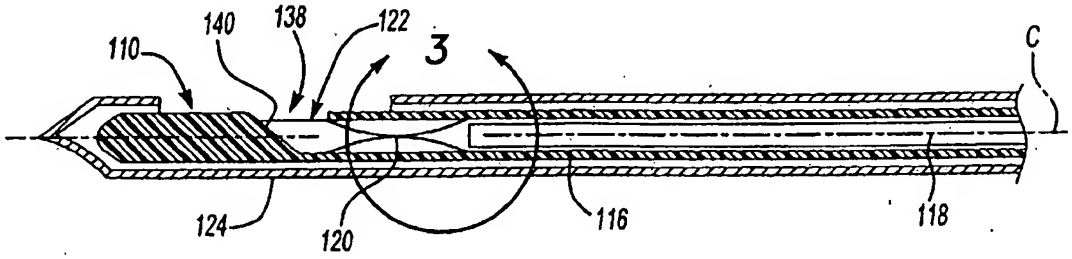

Exhibit B

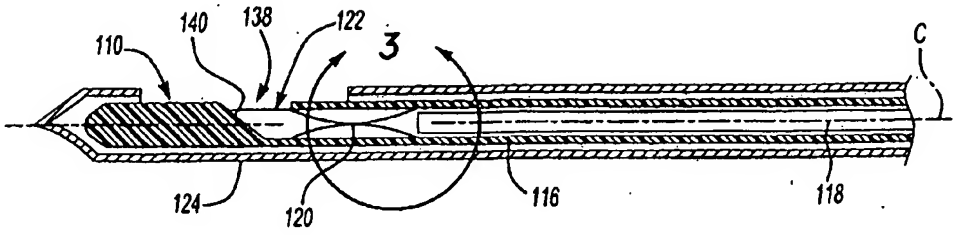

Fig-1

Fig-2A
PRIOR ART

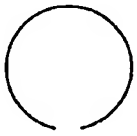

Fig-2B
PRIOR ART

Fig-2C
PRIOR ART

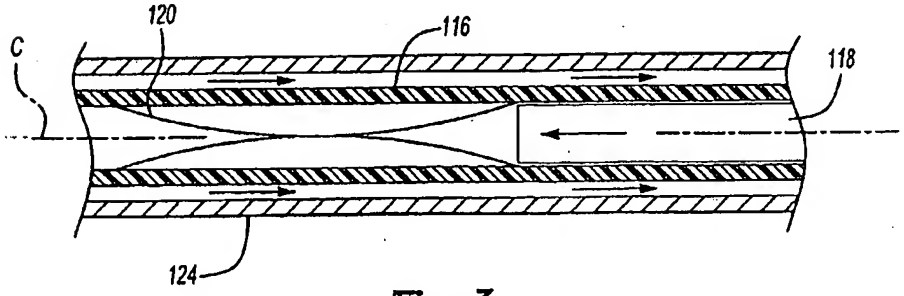

Fig-3

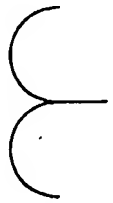

Fig-4A

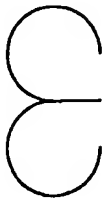

Fig-4B

Fig-4C

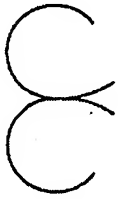

Fig-4D

Fig-5A

Fig-5B

Fig-5C

Fig-6A

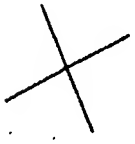

Fig-6B

Fig-6C

Fig-6D

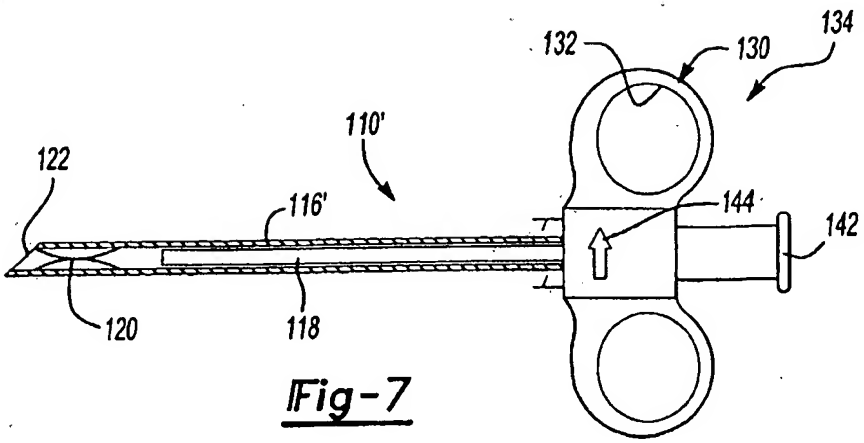

Fig-7

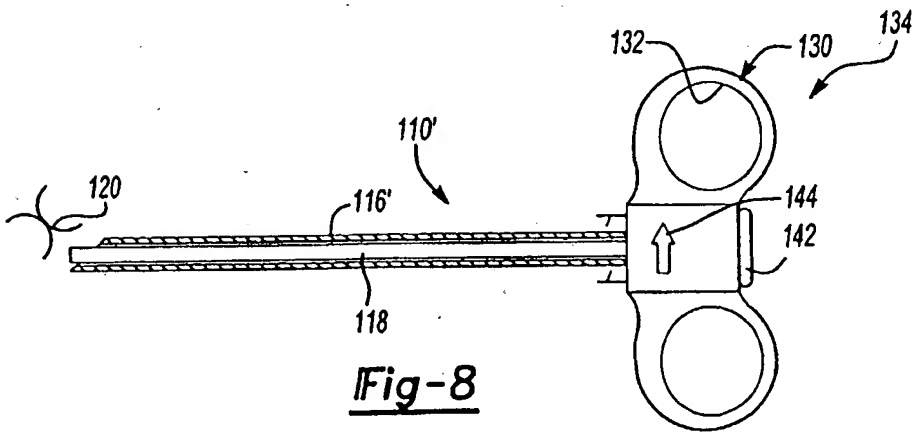

Fig-8

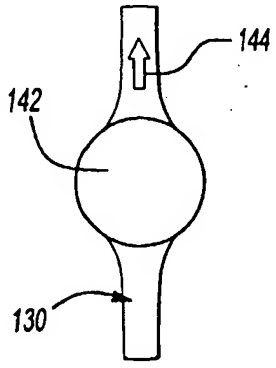

Fig-9

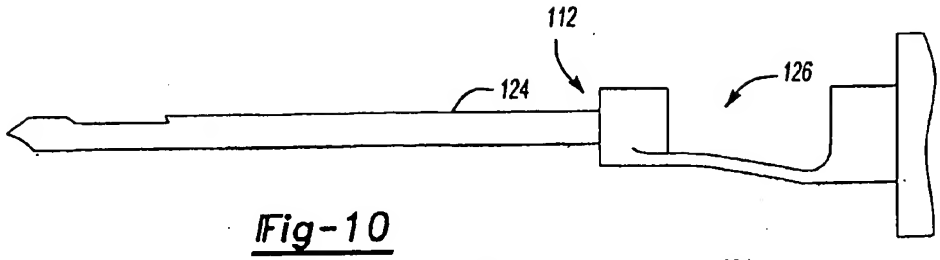

Fig-10

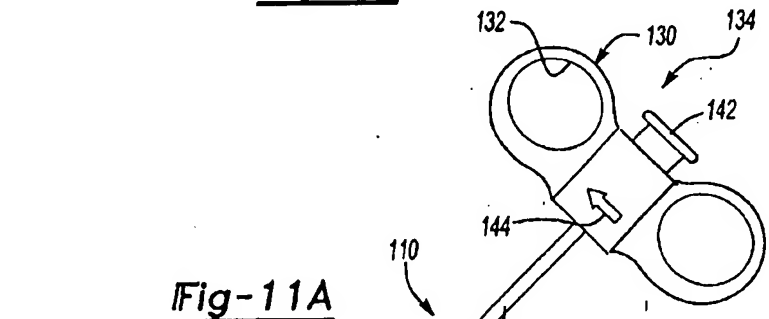

Fig-11A

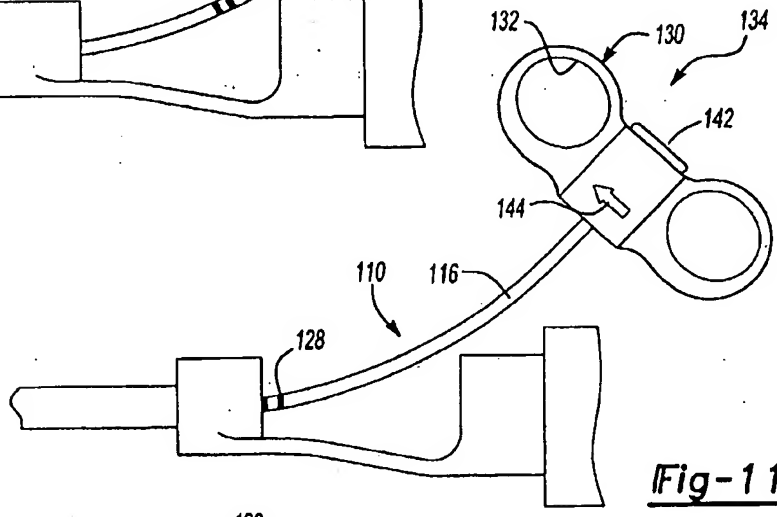

Fig-11B

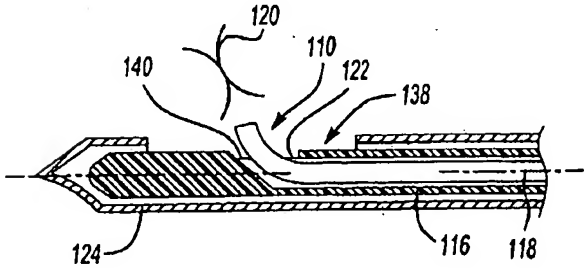

Fig-11C

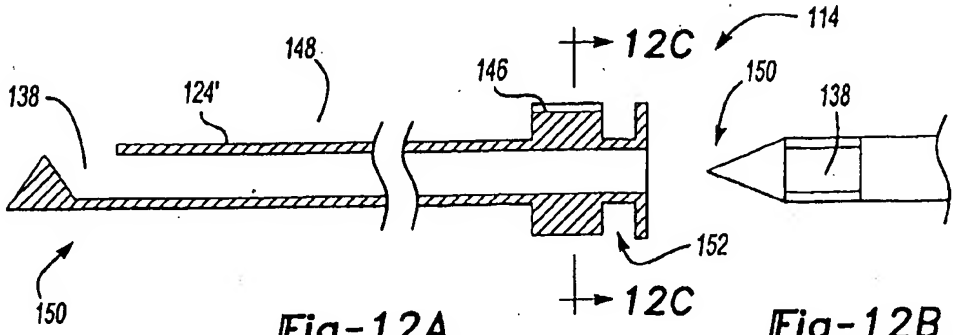

Fig-12A

Fig-12B

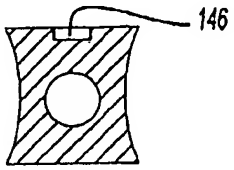

Fig-12C

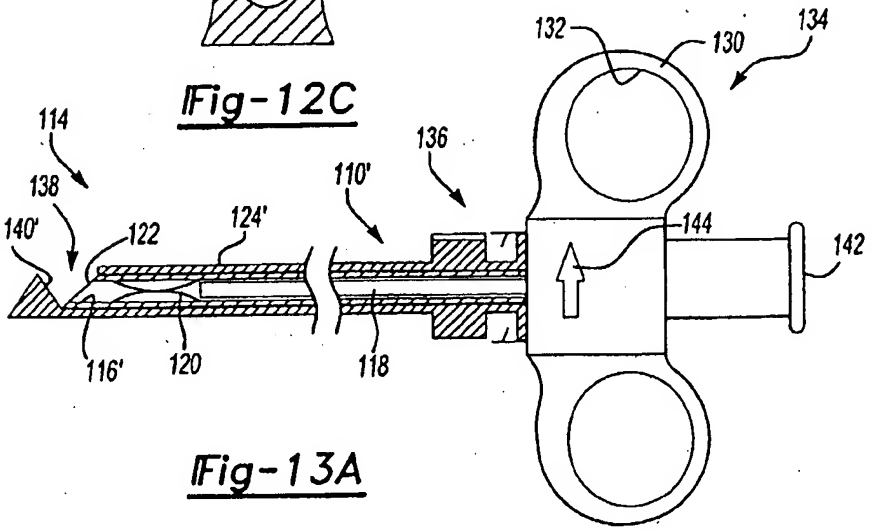

Fig-13A

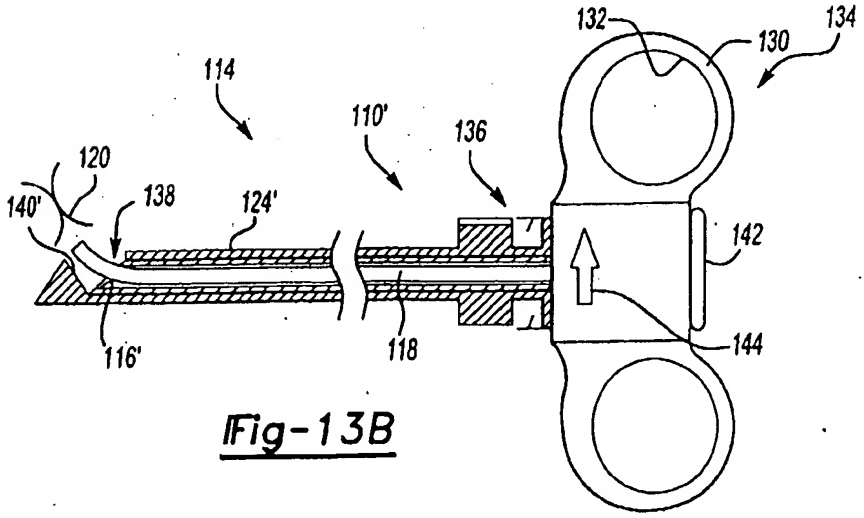

Fig-13B

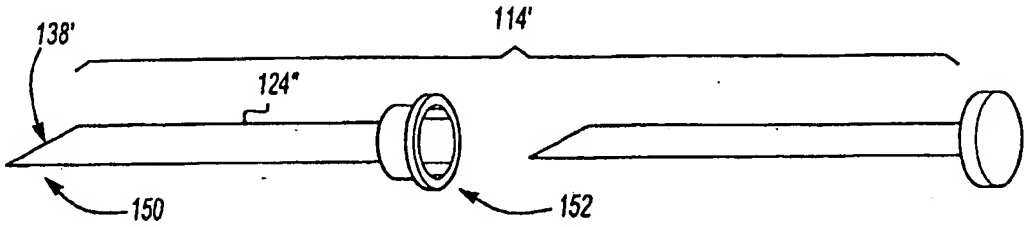

Fig-14

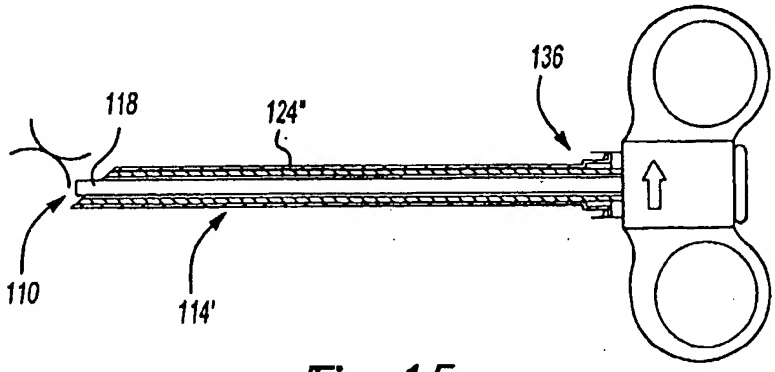

Fig-15

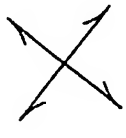

Fig-16A

Fig-16B

Fig-16C

Fig-16D

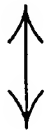

Fig-16E

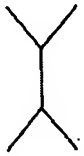

Fig-16F

Fig-16G

Fig-16H

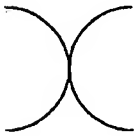

Fig-16I

Fig-16J

Fig-16K

Fig-16L

Fig-16M

Fig-16N

Fig-16O

BIOPSY DEVICES AND METHODS

CLAIM OF BENEFIT OF FILING DATE

[0001] The present application claims the benefit of the filing date of U.S. Provisional Application Serial No. 60/400,113 (filed Aug. 1, 2002), the contents of which are hereby incorporated by reference in their entirety.

TECHNICAL FIELD

[0002] The present invention relates to devices and methods for performing biopsies, and more particularly to breast implantation clips for use as markers in mammography.

BACKGROUND

[0003] Percutaneous biopsy of the breast is a well-accepted alternative to open surgical biopsy with needle localization for those lesions seen by mammography or ultrasound but not able to be felt by the surgeon. When percutaneous biopsy is performed, it is frequently necessary to place a metal clip at the site of biopsy. This is done for several reasons. For example, the lesion biopsied might be partially or entirely removed. If the lesion is proven to be malignant, it is necessary to subsequently do a wide excisional biopsy after needle localization to remove any residual malignancy. The clip makes the site of biopsy apparent, assuring accurate localization. In addition, if something is seen on both mammography and ultrasound, it is not always certain that the lesions are one and the same. A biopsy under ultrasound guidance with placement of a clip allows confirmation by mammography that the lesion is the same or different than the one seen on the mammogram. Further, the presence of a clip seen on a mammogram alerts the radiologist that a biopsy has been performed, prompting the radiologist to more closely evaluate the site of biopsy.

[0004] The vast majority of percutaneous breast biopsies are performed under art-disclosed stereotactic guidance techniques, and generally use a device known as the Mammotome® (by Johnson & Johnson). The clip that is employed is generally prone to pinching a minute amount of breast tissue. Sometimes, the clip may fail to hold onto the tissue or the clip may migrate to a different undesired location.

[0005] U.S. Surgical has produced a clip from a wire with a memory that is delivered into the breast and forms a ring. It is larger in diameter than the Mammotome® device clip and can grab significantly more tissue. The clip is an alloy containing nickel. Recent indications are that U.S. Surgical may no longer manufacture this clip, thus creating a potential supply issue for existing users.

[0006] SenoRx, Inc. produces metal markers embedded in Gelfoam pellets (a product that promotes clotting of blood), called Gel Mark™. The product is packaged to include a plurality of pellets and one radiographic marker. The pellets, however, potentially result in undesired migration of particles.

[0007] Although there is current production of a hand-held Mammotome® device, for the purpose of ultrasound guided biopsy, for some users this device may be awkward and cumbersome to use. The majority of ultrasound-guided biopsies are done with use of Tru-cut needles. This can be done through a coaxial needle. A Bard 12 gauge biopsy needle could be used through an 11 gauge coaxial needle. Through this 11 gauge coaxial needle, a U.S. Surgical clip might also be delivered, although U.S. Surgical is not believed to have marketed their clip for use during ultrasound-guided biopsies.

[0008] Another product is manufactured by Inrad. This clip is used for placement during ultrasound-guided biopsy because the delivery device is steel and does not provide the flexibility necessary for delivery through the Mammotome® needle. This delivery device has a beveled tip, allowing advancement through breast tissue without a coaxial needle.

[0009] Breast biopsies using an 11 gauge coaxial needle have been performed. However, most biopsies are typically done using smaller needles, e.g. a 14 gauge biopsy needle with 13.5 gauge coaxial needle. Such small sizes, in many environments, however, are believed to be too small to efficiently allow advancement of the delivery device of current commercially available clips.

[0010] Turning to another consideration, when a cyst in the breast is aspirated, a spectrum of different types of fluid can be recovered. These might range in color from white to yellow to green or brown. They may be mucousy or bloody and thus can be thick or thin. Some physicians send all samples for cytology analysis, while other physicians may send only grossly suspicious samples (e.g. mucousy or bloody). Regardless of which cyst fluids are sent for cytology, once a cyst is evacuated or in the event that a cyst cannot be fully evacuated because it contains a solid component, a radiologist would like to place a clip into the lesion. It is often important to mark the cyst so that should the cytology prove malignant, or otherwise require further attention, the exact site of the lesion would be known and a needle localization could be subsequently performed.

[0011] There is a need for improved devices for breast biopsy, cyst aspiration or both, to overcome the above-discussed disadvantages of current commercial products.

[0012] The following United States patents are also useful to more fully understand the context and application of the present invention and are all hereby expressly incorporated by reference herein: U.S. Pat. Nos. 6,161,034; 5,526,822; and 5,649,547. Devices disclosed in the above patents may be modified as desired to incorporate the inventive features disclosed herein.

SUMMARY OF THE INVENTION

[0013] In one aspect, the present invention meets the above needs by providing an improved clip for mammography analysis, comprising a first portion that is straight, arcuate or a combination thereof; and at least a second portion that is straight, arcuate or a combination thereof, and which is connected to the first arcuate portion at an apex, wherein the first and second portions are adapted to be compressed to fit within a tube of a delivery device and to elastically deform relative to each other upon exiting the tube for engaging tissue.

[0014] In another aspect the present invention contemplates an improved device, preferably of compact design, for performing a breast biopsy, marking an aspirated cyst, or both, comprising a gripping portion including finger rests attached to a hub portion; a tube having defined at one end portion a hole; and a driver having an actuator member in

driving relation therewith; wherein upon translation of the actuator member the driver advances in the tube to advance any clip located in the tube for expulsion through hole, and further wherein the actuator requires only one hand to deploy the clip from the clip delivery portion and is substantially free of a lock that requires unlocking to permit the actuator to operate.

[0015] In yet another aspect of the invention, there is contemplated a device and a method for marking an evacuated cyst, such as a breast cyst, comprising the steps of inserting a needle into a fluid filled cyst (e.g. a breast cyst); removing fluid from the cyst for collapsing the walls of the cyst; and inserting a clip as a marker into the cyst using the needle.

DESCRIPTION OF THE DRAWINGS

[0016] **FIG. 1** illustrates a side view of an illustrative system which is suitable for use to deploy clips in accordance with the present invention including a clip delivery device in combination with a biopsy instrument.

[0017] FIGS. 2A-2C illustrate prior alternative configurations for clips.

[0018] **FIG. 3** illustrates an enlarged section of **FIG. 1** showing deployment of a clip of the present invention through a deployment tube of a clip delivery device within a biopsy instrument.

[0019] FIGS. 4A-4D, illustrate alternative configurations for clips of the present invention in their deployed state.

[0020] **FIG. 5A** illustrates an alternative configuration for a clip of the present invention in its deployed state.

[0021] **FIG. 5B** is an end view of the clip of **FIG. 5A**.

[0022] **FIG. 5C** is an example of an alternative end view of a clip of **FIG. 5**, in which the ends are rotated relative to each other for achieving a three dimensional configuration in a deployed state.

[0023] FIGS. 6A-6D illustrate alternative configurations for clips of the present invention in their deployed state.

[0024] FIGS. 7-8 illustrate a rigid shafted clip delivery device respectively in pre- and post-deployment states.

[0025] **FIG. 9** is an end view of the device of **FIGS. 7 and 8**.

[0026] **FIGS. 10, 11A** and 11B illustrate a plan view of a biopsy instrument useful in combination with a clip delivery device of the present invention.

[0027] **FIG. 11C** illustrates a side section view of a biopsy instrument of **FIGS. 10, 11A** and 11B.

[0028] **FIG. 12A** is a side section view of another alternative device to illustrate a preferred breast cyst aspiration needle device.

[0029] **FIG. 12B** is a top plan view of an end portion of the embodiment of **FIG. 12**.

[0030] **FIG. 12C** is a sectional view taken through lines 12C-12C of **FIG. 12A**.

[0031] **FIGS. 13A and 13B** illustrate a side section view of another alternative device to illustrate a preferred cyst aspiration needle device with a side hole in combination with a coaxially inserted clip delivery device.

[0032] **FIG. 14** is an example of an alternative cyst aspiration needle with an end hole.

[0033] **FIG. 15** is an example of clip delivery device employed in combination with an aspiration needle as in **FIG. 14**.

[0034] FIGS. 16A-O illustrate yet further examples of alternative clips in accordance with the present invention.

DETAILED DESCRIPTION OF THE PREFERRED EMBODIMENT

[0035] The present invention is directed to improved devices and methods for medical diagnosis and treatment, and particularly devices that are employed for mammographic analysis, such as for the detection and treatment of cancerous or other abnormal growths. The present invention contemplates an improved clip, such as for use as a marker, a delivery device for deploying the clip, a cyst aspiration device, combinations thereof and methods of using the same.

[0036] As will be seen from the description that follows, the various inventive features are not confined to a single application, but rather are capable of numerous variations. Accordingly, though described in a certain context, as will be apparent, features may be interchangeable among embodiments. For sake of brevity, while still providing ample instruction to the skilled artisan, the features herein are described without limitation in embodiments featuring the employment of a clip delivery device **110 (110')** by itself, with a biopsy instrument **112**, such as a vacuum assisted instrument or a cyst aspiration device **114 (114')** or combinations thereof. Accordingly, it is contemplated that the clip delivery device may deploy a clip through an end hole or a side hole of a rigid, semi-rigid or flexible tube, and possibly thereafter through an end hole or a side hole of an outer needle (which itself may be a part of an integrated or separately connectable device and may be rigid, semi-rigid or flexible).

[0037] In general, one common feature of a number of the different embodiments herein is the use to precisely deploy clips directly at a biopsy site, the site of an aspirated cyst, or any other desired site, and thus be able to accurately and reliably mark the site with the clip, as will be demnonstrated by the various embodiments herein, and particularly taking into account the alternative clip designs of FIGS. 4A-4D, 5A-5C, 6A-6D and 16A-16O.

[0038] As seen from those drawings the clips typically are a relatively fine structure, and are contemplated as commonly being made of a wire, such as a surgical stainless steel wire, a titanium wire, nickel containing metals, a biocompatible polymer or the like. Of course, other biocompatible materials may likewise be employed, such as, other non-corrosive materials or otherwise.

[0039] In one aspect of the present invention, the clip may be delivered through a system or according to a method that uses a biopsy instrument such as a Mammotome® vacuum-assisted biopsy instrument, available through Johnson & Johnson, pursuant to which a tissue sample may be obtained

with a needle by applying a slight vacuum for drawing, cutting and/or removing tissue.

[0040] In general, any delivery device may be used, whether employed in combination with a suitable biopsy instrument or not. For example, a device might be employed in which a tissue sample is obtained with a needle in combination with a spring loaded mechanism to cut and remove tissue. The clip might also be delivered during open surgery. Preferably any device may be employed for performing mammographic analysis provided it is suitable for stereotactic techniques, ultrasound techniques or a combination thereof.

[0041] It is contemplated that the delivery device includes an actuator portion that may be removably associated with the delivery device, the biopsy instrument or both. Thus, for example, one preferred apparatus may include a biopsy instrument that includes a needle portion that is insertable into a patient. Coupled with or within the needle portion, or integrally defined as part of the needle portion may be a cutter (e.g., a movable needle that can be manually driven, driven by a motor, or both), a vacuum device or a combination thereof.

[0042] In some embodiments, accordingly, the delivery device of the present invention is flexible over at least a portion of its length to provide better maneuverability through a tissue mass or otherwise. Therefore, it is foreseeable that at least a portion of the delivery device is made of plastic or another flexible material. However, the present invention also contemplates the use of a rigid delivery device comprising a harder material such as a rigid plastic, metal or otherwise. Combinations of different materials may, of course, be employed as desired.

[0043] Referring to **FIG. 1**, one example of a system is illustrated as comprising a clip delivery device **110** that includes a delivery tube **116** (which optionally may be open, such as by a longitudinal groove, notch, slot or aperture at an end or over at least a portion of its length, and is illustrated as having a blunt tip and a side hole) and a driver **118**. A portion of the driver **118** is configured to slide within the delivery tube **116** and push an object, such as a clip **120** (shown in an undeployed state) or otherwise out of a tube exit opening **122**. As shown in **FIG. 1**, the system includes a portion of a biopsy instrument, particularly one including a needle **124**. Referring also to **FIGS. 10, 11A** and **11B**, one such biopsy instrument **112** may include a window portion **126** into which the delivery tube **116** of the clip delivery device **110** can be axially inserted, such as to a predetermined location as suitably defined by a visual indicator **128**.

[0044] Referring again to **FIGS. 10, 11A** and **11B**, preferably, the clip delivery device **110** further comprises a gripping portion **130** having a finger rest **132** and a hub portion **134** affixed, integrated with or otherwise attached to the tube, driver or both. The gripping portion may be enclosed as shown, or it may be open. It may be adapted for receiving a single finger or a plurality of fingers.

[0045] As seen, advantageously, the clip delivery device **110 (110')** may further comprise or be integrated or used with an aspiration needle device, which may be open at an end or over at least a portion of its length. The aspiration needle device may comprise a separable unit configured to temporarily receive the tube **116 (116')** of the device **110 (110')**, or alternatively, the aspiration needle device, the tube **116 (116')**, or both may be formed with, permanently or temporarily attached to a portion of the delivery device **110 (110')**.

[0046] For example, one such suitable attachment feature might include a luer lock or other suitable attachment mechanism, which would permit a user to readily assemble or disassemble components. For example, without limitation, as depicted more particularly in FIGS. **12A-12C** and **13A** and **13B**, it is contemplated that a connecting portion **152** connects the needle or device to a luer lock connector **136** associated with the clip delivery device **110'**. See also **FIG. 15**. The needle, the tube or both may be connected with such an attachment mechanism.

[0047] Alternatively, the aspiration needle device **114 (114')**, tube **116** or both may be affixed to the delivery device **110'** using an adhesive, through welding (e.g., friction welding), integrally formed or otherwise. Preferably, when combined together (as seen alternatively, for instance, in the various embodiments of **FIGS. 1, 311A-11C, 13A, 13B, 14** and **15**), the needle **124 (124')** and the tube **116** will be coaxially aligned about a center line such as center line "C". The coaxially alignment may be created using the attachment device for the needle (e.g., luer lock or otherwise) or it may be created other structural alignment features such as a mating configuration between the end portions of the needle and the tube. Such a needle would typically be configured with a needle opening **138**, an open end or otherwise so that any needle opening would be aligned with the tube opening **122**, as in **FIG. 1**. With the addition of a needle **124** to the delivery device **110**, it is possible to perform additional functions such as excise, aspirate or otherwise manipulate a portion of a tissue sample.

[0048] In any of the examples contained herein, it is foreseeable that a clip **120** is compressed upon itself and inserted into the tube portion **116 (116')** of the delivery device **110 (110')** at some point prior to the use of the same. As such, the clip may be inserted into the tube at any time from the manufacture of the tube or up until just prior to the use of the delivery device. It is further contemplated that the clip may comprise a separately manufactured component, as described in greater detail herein, or it may be a removable portion of the delivery tube or any other portion of the delivery device.

[0049] Also, it is contemplated that more than one clip may be loaded within a single delivery device. For example, the delivery device may be configured with a plurality of clips compressed upon themselves and located within the delivery tube, needle, or otherwise. As such, it would be possible to insert more than one clip into a breast, either at similar or different locations, using a single delivery device.

[0050] As can be appreciated, the device **110** is inserted into a tissue sample, such as a breast or otherwise, and the end portion including the tube **116**, the needle **124** or both, is positioned to the portion of the tissue that is of interest. Once positioned, manipulation of the tissue may be performed by, for example, providing a vacuum through a portion of the needle **124'**, tube **116'** or otherwise, to pull the tissue into the needle opening **138**. Advantageously, the vacuum force may be used to assist in excising a portion of the tissue for pathological analysis or otherwise. It should be

appreciated that in addition to the above described structure any suitable additional blade configuration may also be employed.

[0051] Either before or after the excising or aspiration of the tissue, a clip **120** may be deployed through the tube opening **122** and needle opening **138**, if present. The device and/or needle may then be rotated (e.g., from about 90 to about 270°, and more preferably about 180°) so when it is withdrawn, the needle opening **138** does not hook or otherwise catch onto the clip **120** and accidentally dislodge it.

[0052] In certain embodiments, such as shown in **FIGS. 1 and 11-13**, the delivery tube, the needle or both has a guide surface such as a ramp **140 (140')** on the inside that directs the clip **120** out of the tube opening. However, alternatively the delivery device may comprise a rigid or semi-rigid tube having a tube opening directly defining the axial end of the tube, for delivery of a clip. With this alternate configuration, it is foreseeable that the tube is shaped or comprises needle-like characteristics for allowing the insertion directly into tissue.

[0053] As best seen in **FIGS. 1, 3** and **11** (with reference to clip deployment with a biopsy instrument having a needle **124**, such as a vacuum assisted biopsy instrument), **FIGS. 7 and 8** (with reference to clip deployment independent of an additional biopsy instrument), and **FIGS. 13A, 13B** and **15** (with reference to clip deployment in combination with a cyst aspiration needle device), the deployment of the clip comprises advancing (e.g., by sliding) the clip within the tube using a suitable driver **118**. To fully deploy the clip within the tissue of interest, the driver extends to the end of the tube and, if desired, then through tube opening and any needle opening, if present. This ensures that the clip **120** is free from both the delivery device and the needle **124 (124')** prior to withdrawal or rotation. Though the driver **118** is applying a force to advance the clip within the tube, in a highly preferred embodiment, it should be appreciated that it does not impart any significant force to the clip to cause the clip to elastically deform about itself upon exiting the delivery device.

[0054] The driver **118** may be solid along its length, or at least partially hollow. As such, it is foreseeable that the channel within the drives may be used to provide a path for fluid, instruments or otherwise. It may be coated or uncoated. For example, it may have a low friction material over an outer surface.

[0055] In one embodiment (e.g., as shown in **FIGS. 7 and 8**), for the clip **120** to be delivered under ultrasound-guidance (e.g. employing a suitable ultrasound instrument), it is advantageous for the delivery device **110'** to include a rigid tube **116** (e.g., made of a steel) and the tip to be beveled.

[0056] One benefit of the present invention is that clip deployment can be accomplished with or without a vacuum assist. Precise location of a clip relative to the biopsied region is possible, and it is also possible that the clip can be deployed to the exact location of the biopsy.

[0057] It will be appreciated that, particularly for mammographic analysis, the area biopsied can sometimes be very small. Also, after biopsying a lesion, the lesion potentially might become obscured by bleeding. As such, it may be desirable for the coaxial needle **124 (124')** to be at least temporarily left in place so that it serves as a valuable landmark for the accurate placement of the clip **120**. Thus the present invention contemplates a step of temporarily placing a needle (e.g., a 13 gauge needle or another needle, preferably open at both ends) in the biopsy region prior to deployment of a clip. Thereafter, the tube of the delivery device is inserted into the needle for deployment of the clip.

[0058] Though preferred delivery devices are disclosed herein, such disclosure is not intended to foreclose the adaptation and use of other devices. Additional examples of delivery devices for use herein are described without limitation in U.S. Pat. Nos. 5,526,822; and 5,649,547, hereby incorporated by reference.

[0059] The design of the clips **120** helps to avoid the possibility of migration. That is upon deployment, the ends of the one or plurality of wires are such that they catch and attach to the tissue, such as by unfolding upon itself (e.g., by rotating at least 45° relative to an opposing portion, such as about its apex, more preferably at least 60°, still more preferably greater than 90°, and possibly greater than 180°), and employing its intrinsic elasticity to force an end of the clip into the tissue. Preferably the stored energy of a clip as it resides (e.g., in a compressed state relative to its relaxed state) within the clip delivery device prior to deployment is sufficient that it can unfold upon itself and penetrate tissue in the absence of an externally applied force, as is common with prior clip devices, such as **FIG. 2A** (which generally employs a detachable tensioning wire). Nonetheless, the shape of the clip is such that uncontrollable spiraling, which might lead to undesired migration can be avoided.

[0060] Accordingly, as the wire of the clip progresses to its relaxed state, upon exiting the delivery device **110**, it is capable of pulling the clip **120** by itself (i.e., under its own stored energy and preferably in the absence of additional user-applied energy) into position, assuring secure deployment and substantially preventing migration.

[0061] Various examples of clips **120** useful in accordance with the present invention are shown, without limitation, in FIGS. **4A-6D** and FIGS. **16A-160**.

[0062] In one set of examples of a preferred clip **120**, arcuate portions (e.g. FIGS. 4A-D, 6A, 16C, 16D, 16G, 16I, 16J and 16Q) may be joined at an apex, or a plurality of apexes, to form a clip of the present invention. Alternatively, in another set of examples of a preferred clip, the clip **120** of the present invention may include straight portions (e.g. FIGS. 5A, 6B-D, 16A, 16B, 16E, 16F, 16H and 16K-N) joined at an apex or a plurality of apexes. It is further contemplated that any of the above clip examples may be combined with any other clips, or the same clip, to form yet more examples of a clip **120** of the present invention. Furthermore, all of the above clips **120** may further comprise additional features, which may be resistant to migration through a breast, such as a barb as in FIGS. 16A-E and 16H, 16K and 16L.

[0063] In another aspect of the present invention, a preferred delivery device **110** of the present invention comprises an actuator **142** as seen in **FIGS. 7, 8, 11A, 11B, 13A** and **13B**, which is compact in design and is useful by itself or in combination with another biopsy instrument such as has been described for performing either or both of the percutaneous or ultrasound guidance techniques. A preferred

driver **118** comprises a pushrod or piston like configuration, wherein the actuator **142** applies a force to one end thereby driving the piston or pushrod through the tube along with any clip contained therein. However other driver and actuator configurations are available and contemplated, as well known in the art of tissue aspiration and excising.

[0064] Advantageously, the design of a preferred gripping portion **130** (e.g., handle, or otherwise) and deployment actuator **142** of the present invention requires only one hand, either left or right (e.g. the devices are designed for ambidextrous use), to deploy the clip **120**. Further, though a lock may be employed, a preferred delivery device **110 (110')** has no lock that requires unlocking. Instead, there may be incorporated some slackness or other approach for providing initial "play" when actuating the actuator **142** (such as by pressing a button, squeezing a trigger or the like) before which the clip is deployed. This can be accomplished with a suitable driver, for example, with a suitable cable, or more preferably by a push rod (e.g., having a length that is slightly shorter than the shaft in which it is disposed). In this manner it is possible to gain further control to help avoid accidental deployment of the clip.

[0065] As illustrated in the embodiments of FIGS. **8-12**, a preferred gripping portion **130** will have a suitable grip portion, such as one that has finger rests **132** (e.g., at least one and preferably two opposing open or generally semi-circular finger grips or substantially entirely enclosed circular finger grips) that help secure control, for either left or right-handed operators. As seen, for example in **FIGS. 7, 8, 11A, 11B, 13A, 13B** and **15**, in one preferred approach for the device, the gripping portion **130** optionally may be configured with a surface marking **144** (e.g., an arrow, text, or otherwise) pointing toward the direction of the tube opening or needle opening, indicating the direction in which a clip will be deployed from the device.

[0066] Additionally locator features may also be employed. For example, as shown in FIGS. **12A-13B**, a notch **146** might be employed to help align the gripping portion with a needle or other component that is separably attached, such as by way of a luer lock.

[0067] **FIGS. 7 and 8**, and **FIGS. 13A and 13B** illustrate side views of an example of a preferred gripping portion **130** and deployment actuator **142** of the present invention, shown in illustrative pre-deployed **(FIGS. 7 and 13A)** and deployed **(FIGS. 8 and 13B)** conditions.

[0068] Once the button of the actuator **142** is depressed completely and the clip **120** has been fully deployed, the button of the actuator may include a feature for automatically locking it into a depressed position, providing feedback to the physician that the clip has been fully deployed. For example, a detent, an over center lock, a snap, or the like locking mechanism, might be employed in the gripping portion which is engaged only upon deployment. Upon locking of the locking mechanism, there is an audible sound and/or just prior to locking there is slight increased resistance, which must be overcome, providing palpable feedback that the clip has been fully deployed.

[0069] The actuator **142** may further comprise a return device (not shown) for retracting the end portion of the driver back within the tube. As such, a return device (e.g., a spring or otherwise) may bias the movement of the actuator **142** so that upon release of the same the actuator will retract to predetermined position (e.g., a stop position, a lock portion, an indentation or projection, the original position or otherwise). By retracting the driver into the tube, the clip will be substantially free from the device and will not catch or otherwise be dislodged from the insert position during rotation or withdrawal of the needle from the object into which it is inserted.

[0070] The tube and/or needle associated with any delivery device herein may employ a flexible shaft or a rigid shaft or a combination thereof. It may be made of a suitable metal (e.g., surgical steel, titanium or the like), plastic or other material. It may be coated or uncoated, transparent, opaque or combinations thereof.

[0071] The actuator of the present invention may optionally include a hub portion that is adapted for temporary or permanent connection with a shaft, tube or the like. For example, as seen in **FIG. 15**, a fitting **136** (e.g., a Luer lock fitting) is provided for attachment of a needle or other projection with the hub portion of the actuator.

[0072] With reference now to FIGS. **12A-15**, there are shown alternative embodiments contemplated within the present invention, in which a cyst aspiration device **114 (114')** is employed, and preferably one through which a clip **120** could be deployed. Examples of needles **124' (124")** are shown in FIGS. **12A-12C, 13A, 13B, 14** and **15**. For instance, the needle preferably includes a shaft **148** (e.g., metal such as steel or titanium, plastic or the like), with a cutting portion **150** (e.g., having a tapered tip) and a connecting portion **152**. Though an end hole **138'** may be employed (as seen in **FIGS. 14 and 15**), the cutting portion **150** in FIGS. **12A-13B** is preferably configured with a side hole **138** that will align with a fixed or displaceable cutting edge (e.g., a bevel on a stylet). Thus, a stylet or other device may also be employed for cutting tissue, preventing tissue from filling the needle before aspirating a cyst, or both.

[0073] As seen, the use of a typical Luer lock **136** or other suitable end fitting at the connecting portion preferably allows ease of use with readily available syringes or with an actuator **142** such as described in the above (e.g., with or without finger holes) for delivering a clip **120**. It also allows for removal of the actuator **142** while retaining a needle in place. Thus it is possible that a clip is loaded into the device after the needle is inserted into the patient.

[0074] The gauge of any aspiration needle **124' (124")** of the present invention may be substantially the same as or larger than the gauge of conventional needles available for cyst aspiration, it being recognized that frequently the fluid is thick and will not be able to be practically withdrawn through a typical 19-gauge needle, in the absence of a thinning protocol (which might be employed, such as by chemistry, thermally, or otherwise). A larger gauge, e.g., about 15 to about 18 gauge is preferred in one particular embodiment for evacuating cysts.

[0075] Also, the needle lengths of the present invention may vary as well. For example, the needle may be configured having a length from about 1 cm to about 10 cm and, in one embodiment, more preferably about 2 to about 5 cm; and more preferably about 5 to 10 cm in another embodiment.

[0076] At times, having a needle with a long length can prove to be an advantage. For example, cysts are sometimes

deeper than can be reached with a 2-cm blood-drawing needle. As such, the needle of the present invention would be produced in one or more lengths and gauges that would precisely match the steel shafted breast marking clip device. The length or gauge of the needle could be unusual, but matched to the length of the steel deployment device so that other commercially available needles controllably may be used with it, such as with an adapter, the providing of such an adapter also being contemplated as within the scope of the present invention.

[0077] In another aspect of the present invention, if a cyst warrants marking, such as for future examination, a clip could be immediately delivered into the inside of the cyst, while the aspiration needle remains in place. The aspiration needle thus also functions as the shaft of a delivery device.

[0078] Furthermore, the device is not limited to use only for evacuated cysts but also could be used for marking solid masses.

[0079] As also discussed further herein, preferred clips should be small enough to fit through any typical coaxial needle that would be used for breast biopsy. This will require that the delivery tube preferably be of a thin-wall construction over a portion of or all of its length (and optionally coated over at least a portion of its exterior or interior surface) so the resulting thickness of the delivery tube for the clip and therefore strength of the shape memory of the wire can be maximized. Of course, this device could then be used either with or without a coaxial needle (which also may be coated over at least a portion of its exterior or interior surface).

[0080] The skilled artisan will appreciate that among the advantages of the present inventive clip design is that is grabs a relatively large amount of tissue. Another advantage of the present inventive clip is that is does not form a spiral configuration. The proposed clip design is thus highly resistant to any accidental migration.

[0081] In use, the present inventive clip design also affords the advantage that, such as using ultrasound guidance, it is possible to place the clip either into the central portion of or next to the mass under consideration for biopsy. It is generally only necessary to see the tip of the needle well and for there to be a positive feel to know that the clip has been deployed.

[0082] Biopsies or mass (e.g., breast cyst) aspirations performed in accordance with the present invention can be performed using any suitable size needle (e.g., 10 to 20 gauge, and more preferably 11 to 15 gauge). Clips of the present invention are preferably of a thickness, diameter or other dimension so that they are capable of passing through the needle. For a wire-based clip, the wire chosen is thus preferably of a smaller gauge than the needle, and more preferably a smaller gauge by a factor of at least one half, so that the wire can be folded upon itself, such as about an apex or flattened for placement into the needle or other tube for delivery. The clips can be hollow cored structures, solid structures (e.g., wire) or filled core structures. They may be coated or uncoated. For example, they may have a pharmaceutical agent over some or all of its outer or inner surfaces.

[0083] For any of the embodiments of the present invention, a line or other marking may be inscribed onto the surface of the needle and/or needle hub as well as onto the surface of the gripping portion and/or hub of the clip device. The lines will allow precise alignment of the needle and device to indicate proper assembly. This would therefore provide confirmation that the opening of the clip device is aligned with the opening of the needle.

[0084] Kits may be provided and used in accordance with the present invention. Examples of components suitable for inclusion in such a kit include, without limitation, one or more of needles, sutures, syringe, anesthetic, sterile wipes, a sharps disposal container, gloves or the like.

[0085] The devices of the present invention preferably will be packaged in a sealed sterile container. The container may include, a transparent wall, an opaque wall or a combination thereof. The devices are preferably used only once and are disposable. In one embodiment, the devices are fabricated with plastic or metal components that can be recycled.

[0086] The present invention also contemplates methods of using the devices disclosed herein. For example, in one embodiment, a method is contemplated for performing a biopsy using a clip of the present invention. In another embodiment, the delivery device herein is used for delivering a clip, such as during a biopsy. The methods discussed in the Background section herein are particularly suitable for use of the devices of the present invention. Thus, the devices of the present invention may be used for percutaneous biopsies, ultrasound guided biopsies or a combination thereof. Kits may be provided and used in performing such procedures.

[0087] The present invention is particularly suitable for mammographic analysis of humans, and particularly female humans, but it is not limited thereto. Without limitation, it can be used for analysis of other human body parts, or for analysis of mammals or other animals other than humans.

[0088] References to the use of a Mammotome® device herein are not intended to foreclose the use of other like devices for performing one or more of the tissue removal, marking or other functions performed by the Mammotome®) device. Accordingly the present invention also contemplates substituting for the Mammotome®) device that is described other such devices, which preferably will have an elongated delivery tube or like structure having chamber through which a clip according to the present invention is advanced, such as by a push rod or the like.

[0089] Though a preferred ejection direction is shown in the accompanying drawings for the deployment of the clips, it is possible to deploy the clips so the apex is the leading portion of the clip.

[0090] Further, in addition to the discussion of the clip contained herein, there may be greater than two straight or arcuate portions for the clips. The straight and arcuate portions can be of the same or different size or shape relative to each other. They may be formed of a single component (e.g., a single wire) or plural components (e.g., plural wires (2, 3 or more wires) such as might result in a structure as in FIGS. 4C, 4D, 5A and others illustrated). The portions need not be arcuate alone or straight alone, but may be straight, or a combination of straight and arcuate. In another embodiment, as seen in FIGS. 5A, 5B and 6B-6D, the clip may be "X" shaped or may have orthogonally disposed arms. The clips alternatively may be "N" shaped, arrows, arcs, tetragonal, or any of a number of different shapes. Combinations of

any of the shapes identified may be employed also. Clips may also include one or a plurality of barbed ends (such as is illustrated by various of the examples provided in **FIG. 16**). When two or more wires are employed they may be configured relative to each other for deployment in a single common plane or over plural different planes. Though larger clips are also possible, when deployed, preferred clips are smaller than about 1 cm in its largest dimension (e.g., length, diameter, etc.), and more preferably, they are on the order of about 5 mm in its largest dimension.

[0091] As illustrated in FIGS. 5A-5C, clips herein may be configured to lie in a single plane (**FIG. 5B**) or include one or more portions that lie in a plurality of different planes, as in **FIG. 5C**.

[0092] Unless stated otherwise, dimensions and geometries of the various structures depicted herein are not intended to be restrictive of the invention, and other dimensions or geometries are possible. Plural structural components can be provided by a single integrated structure. Alternatively, a single integrated structure might be divided into separate plural components. In addition, while a feature of the present invention may have been described in the context of only one of the illustrated embodiments, such feature may be combined with one or more other features of other embodiments, for any given application. For example, the employment of a luer lock may be used in the various embodiments shown to connect components, omitted or substituted with an alternative connector, a guide ramp employed or omitted, side holes might be substituted for end holes, or end holes substituted for side holes, even though such feature might not be shown in the accompanying drawings. Bevel shapes can vary from those depicted. The use of different material combinations than those shown might also be appropriate, such as the substitution of metal for plastic, or plastic for metal. It will also be appreciated from the above that the fabrication of the unique structures herein and the operation thereof also constitute methods in accordance with the present invention.

[0093] The preferred embodiment of the present invention has been disclosed. A person of ordinary skill in the art would realize however, that certain modifications would come within the teachings of this invention. Therefore, the following claims should be studied to determine the true scope and content of the invention.

What is claimed is:

1. An improved clip, comprising:

a. a first portion that is straight, arcuate or a combination thereof; and

b. at least one additional second portion that is straight, arcuate or a combination thereof, and which is connected to the first portion at an apex, the first and second portions adapted to permit the clip to compress to fit within a tube of a delivery device and to elastically deform upon exiting the tube for engaging tissue.

2. The clip of claim 1, wherein the clip is a wire that elastically deforms relative to the apex upon exiting the tube wire, wherein the wire material is selected from a surgical stainless steel, titanium, a nickel containing metal, or a bio-compatible polymer.

3. The clip of claim 2, wherein the clip is adapted to be deployed to a predetermined site in the presence or absence of an applied vacuum.

4. The clip of claim 3, wherein the first or second or both portions are further configured with at least one end having a barbed portion.

5. The clip of claim 1, wherein the clip is made of a memory shape material, has a largest dimension of less than about 1 cm, is configured for insertion into a breast tissue, and wherein upon exiting the delivery device the first and second portions are configured to engage the breast tissue such that the clip becomes substantially immobile and is observable through ultrasound devices, mammography devices or both.

6. An improved device for deploying a clip, comprising:

a. a gripping portion having two opposing finger grips attached to a hub portion;

b. a tube joined with the hub portion, the tube having defined at one end portion a side hole and a ramp or an end hole; and

c. a driver having an actuator member in driving relation therewith; wherein upon translation of the actuator member the driver advances through the hub portion and the tube to advance a clip located in the tube toward and along the ramp for expulsion through the respective hole, wherein the device does not include a lock for preventing deployment.

7. The device of claim 6, wherein the hub portion has a luer lock mechanism for the attachment of the tube to the hub portion.

8. The device of claim 7, further comprising a needle spaced apart and concentrically located about the tube.

9. The device of claim 6, further comprising an indicator for providing physical or audible feedback that any clip has been fully deployed from the tube.

10. The device of claim 6, further comprising a visual indicator to indicate the position of the tube.

11. The device of claim 6, wherein the device is adapted for cyst aspiration.

12. The device of claim 6, further comprising an alignment notch in the hub portion.

13. The device of claim 6, wherein the actuator requires only one hand to deploy the clip from the tube.

14. The device of claim 13, wherein the device is configured to be used ambidextrously.

15. The device of claim 6, wherein the finger grips are semicircular or substantially cirular.

16. The device of claim 6, wherein the clip comprises:

a. a first portion that is straight, arcuate or a combination thereof; and

b. at least one additional second portion that is straight, arcuate or a combination thereof, the first and second portions adapted to fit within the tube of a delivery device and to elastically deform relative to each other upon exiting the tube for engaging tissue.

17. A method for marking an evacuated breast cyst, comprising the steps of:

a. inserting a needle into a fluid filled breast cyst;

b. removing fluid from the breast cyst for collapsing the walls of the breast cyst; and

c. pushing the actuator and driver along the inside portion of the needle resulting in the insertion of a clip into a breast cyst to mark the same; wherein the clip comprises:

i) a first portion that is straight, arcuate or a combination thereof; and

ii) at least one additional second portion that is straight, arcuate or a combination thereof, and which is connected to the first portion at an apex, the first and second portions adapted to fit within a tube of a delivery device and to elastically deform about the apex upon exiting the tube for engaging tissue.

18. The method of claim 17, wherein only one hand is required for the insertion of the needle and the marking of breast cyst and wherein the device is configured to be used ambidextrously.

19. The method of claim 17, wherein the needle has a caliber of 18 gauge or larger and the cyst is aspirated in the absence of a stylet.

20. The method of claim 19, wherein the needle has a side hole for aspirating the cyst, and through which the clip can be deployed.

* * * * *

US006766186B1

(12) **United States Patent**
Hoyns et al.

(10) **Patent No.: US 6,766,186 B1**
(45) **Date of Patent: Jul. 20, 2004**

(54) **POST BIOSPY TISSUE MARKER AND METHOD OF USE**

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(52) **U.S. Cl.** **600/431**; 600/567; 600/167; 606/167
(58) **Field of Search** 600/431, 564, 600/567; 128/897, 898; 606/167, 130

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(57) **ABSTRACT**

An implant for marking a location within the tissue of a patient after biopsy is self-anchoring. In one embodiment a strip of a shape memory alloy such as Nitinol can be straightened to facilitate insertion through a small gauge needle but, once exposed within the tissue to body temperature, assumes a helical coil configuration, thereby mechanically clamping to the tissue. In other embodiments the implants include barbs of resilient, deformable metal which can be straightened for insertion into a small gauge needle, but once the implant exits the forward end of the needle the barbs spring outward, anchoring the implant within the tissue. A method for implanting a plurality of markers within the tissues of a patient involves a needle having a plurality of markers sequentially loaded therewithin. The forward end of the needle is inserted into the tissues of the patient and advanced to a first target location, at which point a first marker is ejected into the tissues of the patient. The forward end of the needle is then relocated to a second target site, and a second marker is ejected into the tissues of the patient.

11 Claims, 6 Drawing Sheets

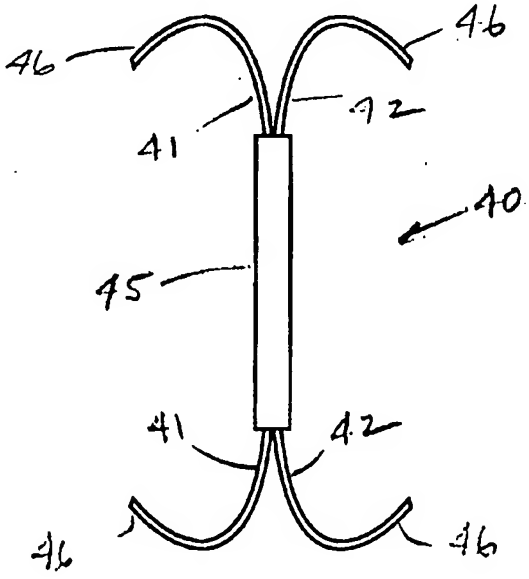

Exhibit C

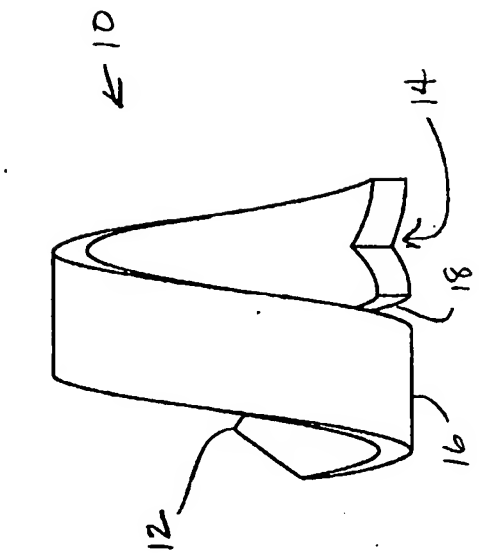

Fig. 2

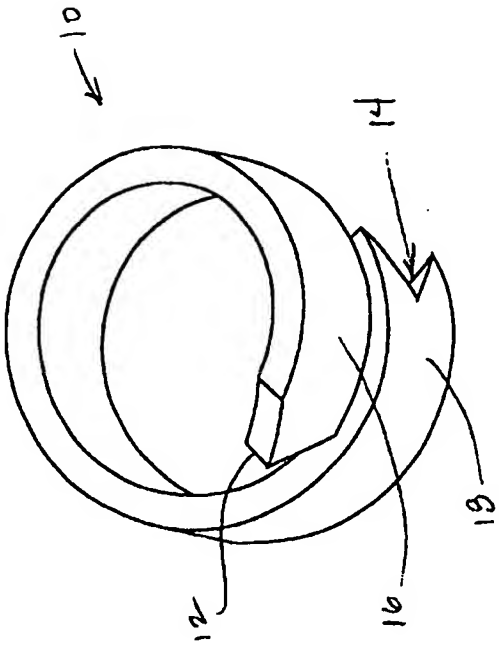

Fig. 1

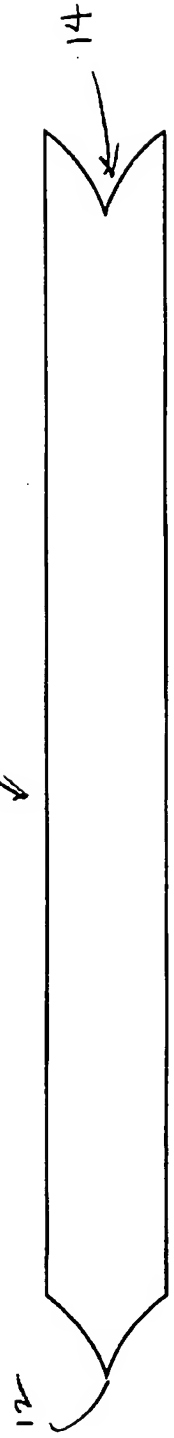

Fig. 3

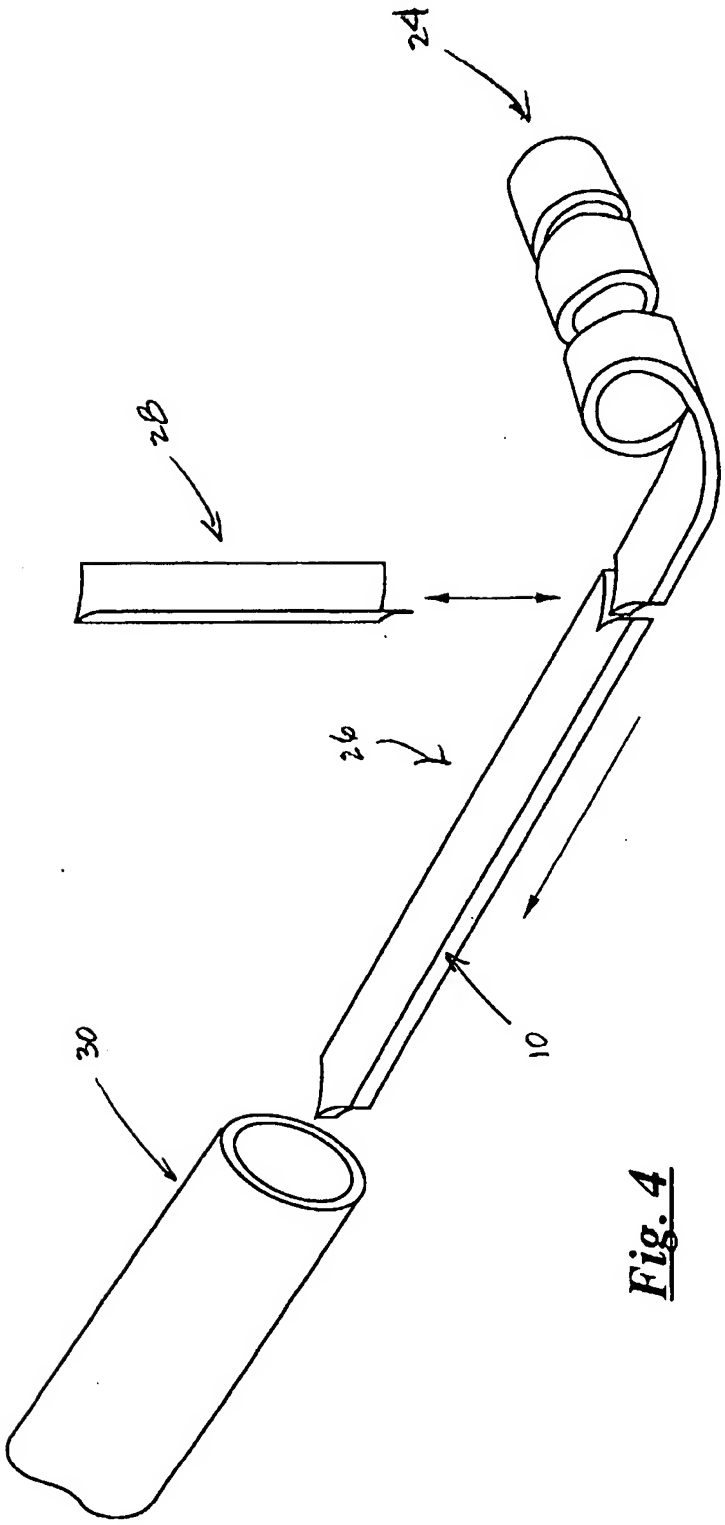

Fig. 4

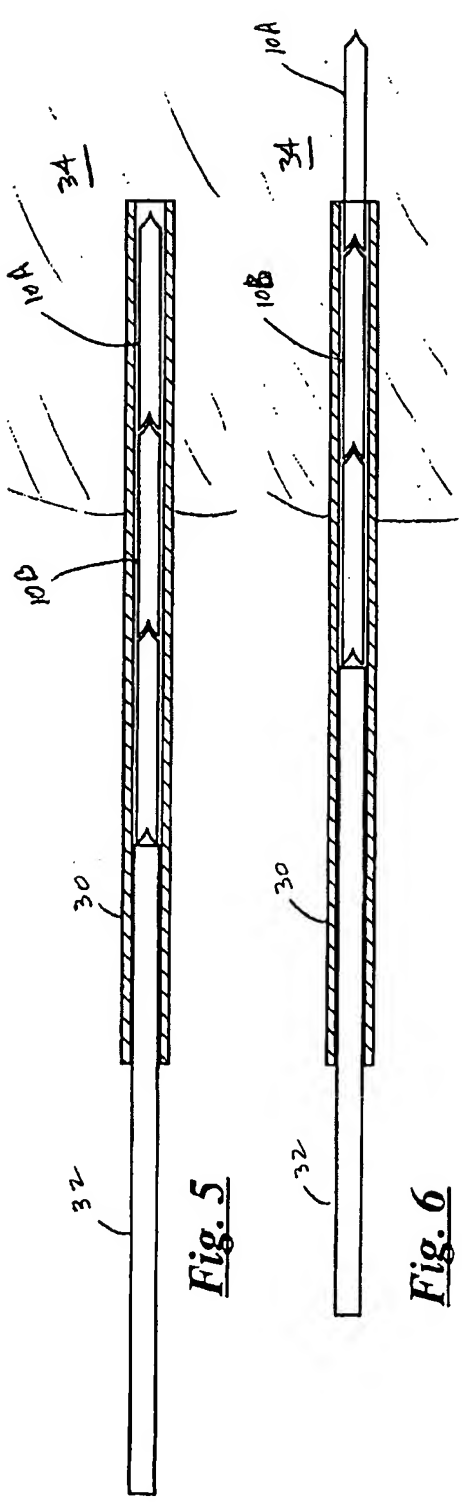

Fig. 5

Fig. 6

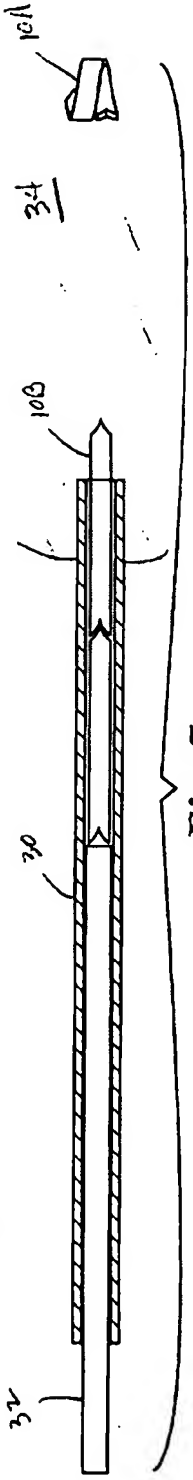

Fig. 7

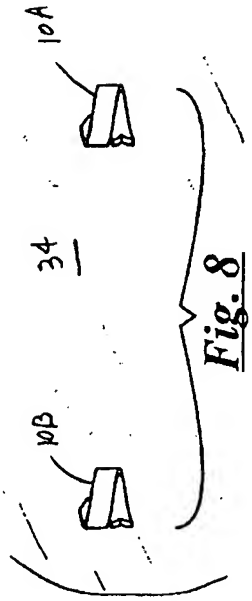

Fig. 8

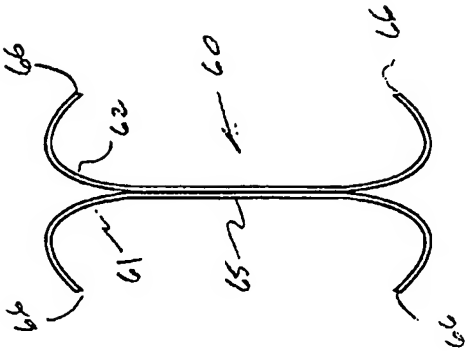

Fig. 14

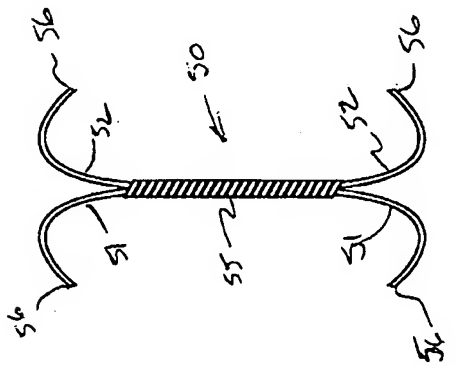

Fig. 13

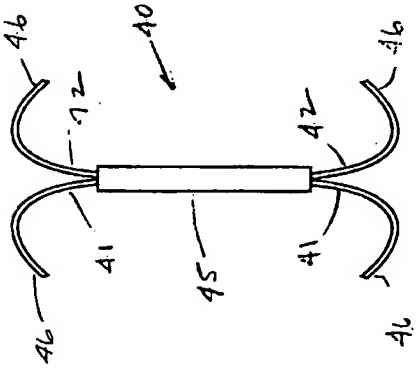

Fig. 9

Fig. 12

Fig. 10

Fig. 11

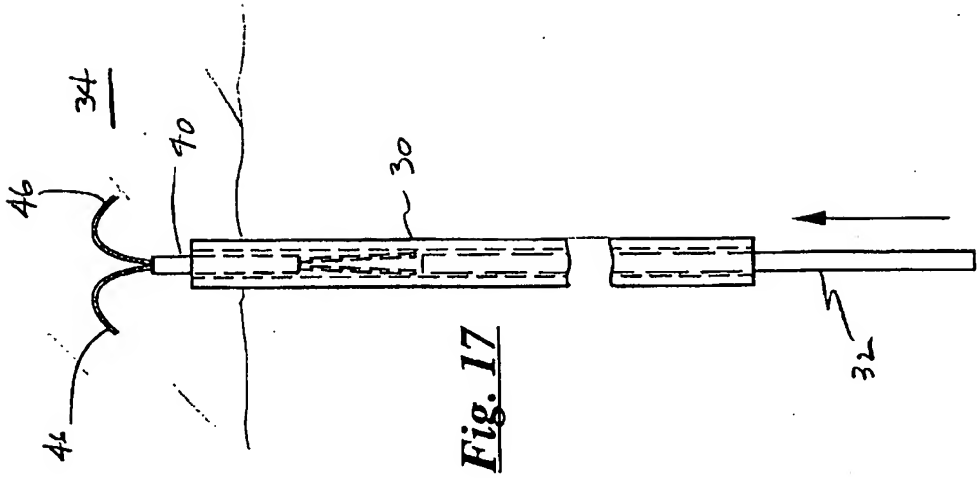

Fig. 17

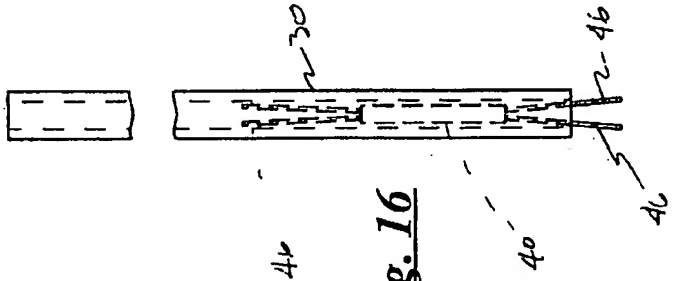

Fig. 16

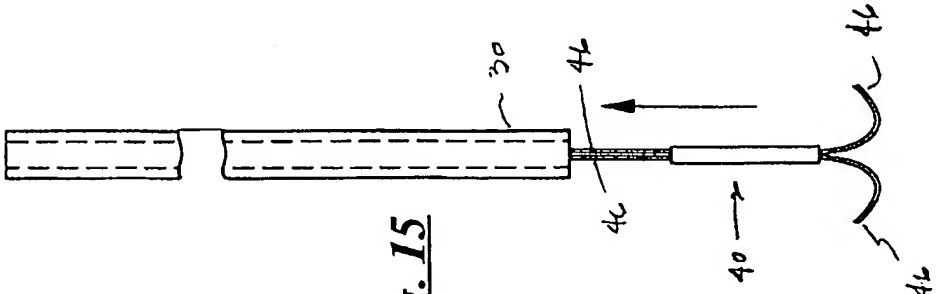

Fig. 15

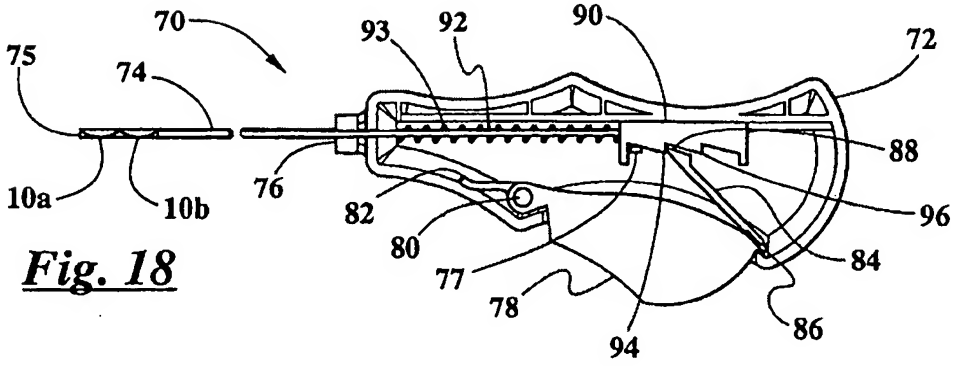

Fig. 18

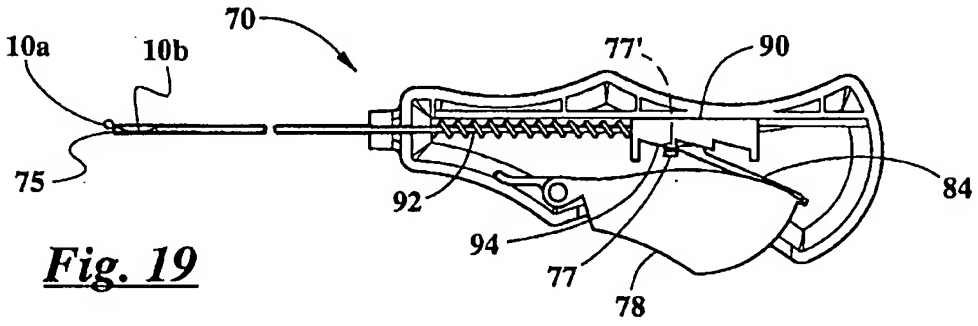

Fig. 19

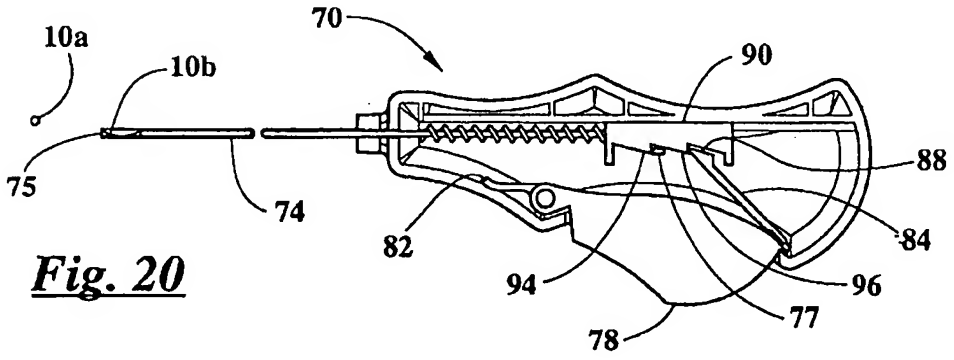

Fig. 20

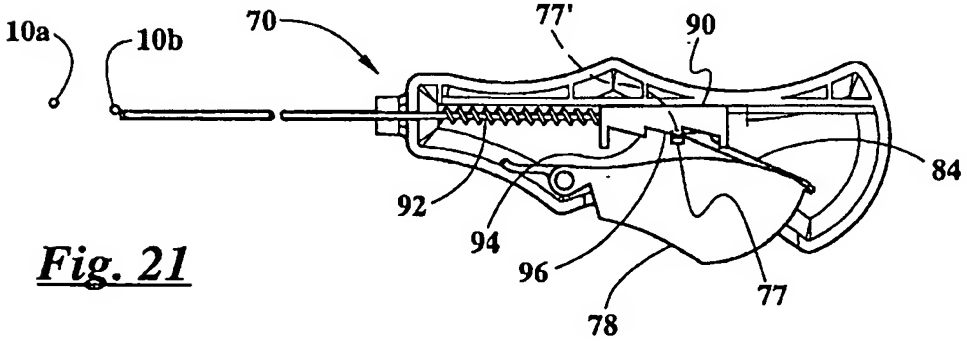

Fig. 21

POST BIOSPY TISSUE MARKER AND METHOD OF USE

TECHNICAL FIELD

The present application relates generally to markers for surgically implanting within the tissues of a patient to mark the location of a lesion. More specifically, the present invention relates to a marker which is mechanically self-anchoring within the target tissue and which can be delivered through a relatively small gauge needle.

BACKGROUND OF THE INVENTION

Advances in modern medical imaging technologies such as X-ray, ultrasound, or magnetic resonance imaging make it possible to identify and to biopsy tumors while they are still small. When dealing with a small tumor, especially after a portion of the tumor has been removed for biopsy, it is sometimes difficult to relocate the tumor at a later time for treatment. This is particularly true in the case of tumors in the breast, where the ability to visualize a small growth may depend upon the manner in which the breast is positioned or compressed during the procedure. In addition, prior to surgically removing a tumor, it is often advantageous to try to shrink the tumor by chemotherapy or irradiation. This is especially true in the case of breast cancer, where conservation of breast tissue is a concern. Shrinkage of the tumor can sometimes make it difficult for the surgeon to locate the tumor. It is therefore often desirable to place a marker within the target tissues at the time of biopsy which can be visualized under a variety of imaging modalities to facilitate finding the tumor at a later time.

For such a marker to be effective, it must be visible under a variety of imaging modalities and must maintain its position within the tissues. Implants placed loose within the tissues have a tendency to migrate, and this tendency is particularly acute in the case of fatty tissue, such as the breast. Accordingly, for such a marker to resist migration, it must clamp or otherwise attach to the target tissues. One device which is currently being used is implanted into the target tissues and then manipulated remotely by means of wires to cause the implant to clamp to the target tissue. However, the manipulation of the wires to clamp the device to the target tissues complicates the deployment procedure. Further, it is possible that the wire may not properly detach from the implant.

Another device which is currently in use involves a C-shaped or U-shaped marker which is implanted and then crimped with a pliers-like instrument to attach the marker to the tissue. However, this process also requires affirmative intervention by the physician beyond simply guiding the marker to the desired location, namely, the step of crimping the marker to anchor it to the tissues. Thus, there is a need for a marker which automatically mechanically attaches to the target tissues upon being deployed, without the need for intervention by the surgeon.

Because of advances in biopsy technology, it is possible to biopsy suspicious tissue with a fourteen or even sixteen gauge or smaller needle. Use of such a small gauge needle minimizes patient discomfort and makes it possible to retrieve the biopsy specimen through a small incision. Since a marker which can be implanted only through a larger needle or incision, or which would require a larger instrument to crimp the anchor to the tissues, would largely defeat the advantages of needle biopsy, there is a need for a marker as well as an apparatus and method for implanting the marker which is capable of implanting and anchoring the marker by way of an instrument no larger in diameter than the needle used for biopsy purposes.

SUMMARY OF THE INVENTION

Stated generally, the present invention comprises a marker for implanting in the tissues of a patient, such as at the time of a biopsy, to facilitate locating the site at a future date. The marker is self-anchoring, automatically mechanically attaching to the target tissues upon being deployed without the need for intervention by the, surgeon. The marker is capable of being implanted through a needle no larger than the needle used for biopsy purposes.

Stated somewhat more specifically, the present invention comprises a marker for inserting by a physician through a lumen of a hollow needle to a target site within the tissues of a patient to facilitate locating the target site at a later time. The marker is capable of assuming an essentially linear configuration for passage through the hollow needle. The marker includes means for anchoring itself to the tissues of the patient without intervention by the physician.

In a first aspect the marker is comprised of a shape memory alloy having a phase change temperature which is higher than normal room temperature but lower than the normal body temperature of the patient. When the marker is exposed to a temperature below the phase change temperature, the marker can be configured into an elongated, essentially linear configuration for passage through the needle. When the marker is exposed to a temperature higher than the phase change temperature, such as by exposure within the tissues of the patient, the marker assumes a predetermined configuration which will anchor it to the tissues of the patient without intervention by the physician. According to one embodiment, the marker assumes a helical shape upon being exposed to a temperature higher than its phase change temperature. In another embodiment the marker assumes a ring shape.

In another aspect, the marker is comprised of a plurality of wires whose free ends form barbs. The barbs are normally bent outward but can be deformed into an essentially linear configuration for passage of the marker through a hollow needle. Upon the marker exiting the forward end of the needle the barbs spring outward, anchoring the marker to the tissue. According to one embodiment, two or more wires are anchored within a tubular body portion with their free ends extending from either end of the tubular body portion to form the barbs. In another embodiment, the central portions of two or more wires are twisted together, with the free ends of the wires forming barbs. In yet another embodiment, the central portions of two or more wires are bonded together, such as by welding, adhesives, heat shrink tubing, or other biocompatible method, with the free ends of the wires configured into barbs.

The invention further includes a method for implanting a plurality of markers within the tissues of a patient. A plurality of markers of the type previously described are sequentially loaded into a hollow needle. A stylet is inserted into the rearward end of the hollow needle to push the markers through the needle and out its forward end. According to the method of the invention the forward end of the needle is positioned at a first location, and the stylet is advanced to eject a first marker from the forward end of the needle and into the tissues of the patient. The forward end of the needle is then repositioned to a second location without withdrawing the needle from the patient, and the stylet is further advanced to eject a second marker from the forward end of the needle and into the tissues of the patient.

Thus it is an object of the present invention to provide an improved marker for implanting in the tissues of a patient, such as at the time of a biopsy, to facilitate locating the site at a future date.

It is another object of the present invention to provide a marker which is automatically self-anchoring without the need for intervention by the surgeon.

Still another object of the present invention is to provide a marker which can be visualized under a variety of imaging modalities and yet which can be implanted through a needle no larger than the needle used for biopsy purposes.

Other objects, features, and advantages of the present invention will become apparent upon reading the following specification, when taken in conjunction with the drawings and the appended claims.

BRIEF DESCRIPTION OF THE DRAWINGS

FIG. 1 is a perspective view of a post biopsy tissue marker according to a first embodiment of the invention.

FIG. 2 is an end view of the tissue marker of FIG. 1.

FIG. 3 shows the tissue marker of FIG.1 uncoiled into an essentially straight configuration to facilitate insertion through a cannula.

FIG. 4 is schematic representation illustrating the fabrication of the tissue marker of FIG. 1 and the loading of the marker into a hollow cannula.

FIGS. 5–8 are schematic representations showing the sequence for implanting the markers of FIG. 1 with a cannula and stylet, with the top half of the cannula removed to reveal interior detail, where:

FIG. 5 shows three of the markers of FIG. 1 loaded within the cannula;

FIG. 6 shows the stylet being advanced to eject the first marker from the forward end of the cannula;

FIG. 7 shows the first marker assuming its helical configuration, the cannula is repositioned, and the stylet is advanced again to eject the second marker; and

FIG. 8 shows the first and second markers clamped within the target tissue and spaced apart relation.

FIG. 9 is a side view of a second embodiment of a post biopsy tissue marker according to the present invention.

FIG. 10 is a top view of the tissue marker of FIG. 9.

FIG. 11 is a top view of an alternate version of the tissue marker of FIG. 9.

FIG. 12 is a top view of another alternate version of the tissue marker of FIG. 9.

FIG. 13 is a side view of another alternate embodiment of a tissue marker according to the present invention.

FIG. 14 is a side view of yet another embodiment of tissue marker according to the present invention.

FIGS. 15–17 schematically represent the procedure for implanting the marker of FIG. 9, where:

FIG. 15 shows the marker being loaded into the rearward end of a cannula;

FIG. 16 shows the marker assuming an essentially linear configuration as it is advanced into the cannula; and

FIG. 17 shows the barbs of the marker springing outward as the marker exits the forward end of the needle to anchor the marker within the tissue.

FIGS. 18–21 illustrate an apparatus and method for implanting the markers of FIG. 9, where

FIG. 18 is a cutaway view of the apparatus loaded with two markers, with the tip of the apparatus positioned at a first target location within the tissues of a patient;

FIG. 19 shows the actuation of the device to discharge a marker into the tissues of a patient at the first target location;

FIG. 20 shows the relocation of the tip of the device to a second target location; and

FIG. 21 shows the actuation of the device to discharge a second marker into the tissues of the patient at the second target location.

DETAILED DESCRIPTION OF THE DISCLOSED EMBODIMENT

Referring now to the drawings, in which like numerals indicate like elements throughout the several views, FIGS. 1–3 illustrate a breast marker **10** according to a first embodiment of the invention. The marker **10** is fabricated from a material that has shape memory properties, such as Nitinol or other biocompatible material that allows for a phase change from the martensitic state to austenitic state at a predetermined transformation temperature. The transformation temperature for the preferred embodiment is approximately 37° C. (98.6° F.), which is nominal human body temperature. Below the transformation temperature the implant **10** can be formed into an essentially linear configuration, as shown in FIG. **3**, to facilitate implantation through a hollow cannula. When the implant **10** is heated to the transformation temperature, such as by exposure within the tissues of a patient, the implant assumes a helical shape, as shown in FIGS. 1 and 2. This shape memory action causes the marker to be "self-closing" or "self-clamping" without any further intervention by the surgeon.

Another reason for fabricating the marker **10** from Nitinol is that Nitinol is radiopaque, ultrasonically opaque, and MRI compatible, meaning it is visible under magnetic resonance imaging without causing artifacts which can obscure visualization of adjacent tissue.

The marker **10** includes a sharpened point **12** at its forward end and a notch **14** at its rearward end. The sharpened point **12** permits the marker **10** to penetrate the target tissue easily. The notch **14** at the rearward end of the marker serves no particular function but is simply the recess left as a result of a point **12** of a contiguous marker **10** being punched from the same strip of metal.

When the marker **10** is heated to its phase change temperature, it assumes the helical configuration of FIGS. **1** and **2**. The helix prescribes an arc of greater than 360° so as to create overlapping portions, **16**, **18**. The overlapping portions **16**, **18** are closely spaced so that when the marker **10** assumes its helical configuration within the target tissue, tissue is clamped between the overlapping portions.

In the disclosed embodiment, the tissue marker in its straightened configuration is 0.250 inches (6.35 mm) long, 0.020 inches (0.5 mm) wide, and 0.006 inches (0.15 mm) thick. In this configuration, the marker fits easily through a sixteen gauge needle. When the marker is in its helical configuration, it has a diameter of approximately 0.060 inches (1.5 mm).

Fabrication of the markers **10** will now be explained with reference to FIG. 4. The markers **10** are fabricated from a helical coil **24** of Nitinol. The manufacturing process takes place at a temperature lower than the phase change temperature of the Nitinol. With the Nitinol in its martensitic phase, the material can be straightened and will essentially maintain the straightened configuration until heated to its phase change temperature. A short length **26** of the end of the coil **24** is straightened and punched with a V-shaped punch **28** to separate a marker **10** from the remainder of the coil.

The V-shaped punch 28 also forms the pointed forward end 12 of the marker 10. The marker 10 is then immediately loaded into the rearward end of a hollow cannula 30. The next section of the coil 24 is then straightened and punched, and the next marker 10 is inserted into the hollow cannula 30 behind the first marker. The markers are not completely straight but retain a slightly bowed configuration, thereby exerting enough interference with the walls of the cannula 30 not to slide freely within the cannula. In the disclosed embodiment, three or four markers 10 are inserted into each cannula 30. A stylet 32 is then inserted into the rearward end of the cannula 30. The markers 10, cannula 30, and stylet 32 are then sterilized and packaged as a unit. The physician thus receives the needle assemblies preloaded with markers, so that the markers never have to be handled once they leave the factory.

Implantation of the markers will now be discussed with reference to FIGS. 5–8. The physician inserts the forward end of the cannula 30 through the same puncture through which the biopsy was taken and advances the tip of the cannula to a location adjacent to the target tissue 34, as shown in FIG. 5. Then, as shown in FIG. 6, the physician advances the stylet 32, forcing the column of markers 10 forward within the cannula 30 and ejecting the front marker 10A out the forward end of the needle and into the target tissue 34. When exposed to body temperature within the target tissue 34, the marker 10A is heated to its phase change temperature and coils into its helical configuration, thereby clamping itself to the target tissue 34. If deployment of a second marker 10 is required, the physician repositions the tip of the cannula 30 and advances the stylet 32 to eject the second marker 10B from the forward end of the cannula, as shown in FIG. 7. After the desired number of markers 10 have been placed in the appropriate locations, the needle assembly is withdrawn, leaving the markers 10 mechanically attached to the target tissues as shown in FIG. 8.

FIGS. 9–14 show alternate embodiments of self-anchoring markers. Rather than utilizing a shape memory metal which will assume a predetermined configuration upon begin exposed to body temperature within the target tissue, the embodiments of FIGS. 9–14 are anchored by means of resilient barbs, which can be straightened into an essentially linear configuration for passage through a cannula and then spring outward upon exiting the forward end of the cannula to anchor the marker within the target tissues.

Referring to FIGS. 9 and 10, a marker 40 includes a pair of wires 41, 42 which are inserted through a short length of tubing 45. The wires 41, 42 are secured to the tubing 45 by welding, soldering, adhesive bonding, crimping the tubing to clamp the wires, or any other suitable biocompatible means. The exposed ends of the wires 41, 42 are bent outward to form barbs 46. In the disclosed embodiment, the tubing 45 is approximately 0.060 inches (1.5 mm) long and 0.050 inches (1.27 mm) in diameter and is formed from stainless steel or other suitable radiopaque, ultrasonically opaque material. The wires 41, 42 are formed from 0.010 inch (0.25 mm) stainless steel, which is one example of a material which has been shown to exhibit the requisite degree of deformability and resiliency. NiTi has also been found to be a suitable material where MRI compatibility is desirable.

The marker 40 is comprised of two wires, each having two free ends, for a total of four barbs 46. As can be seen in FIG. 10, the barbs 46 are all substantially disposed in a common plane. However, it will be appreciated that a greater number of wires can be incorporated into a marker 40 to provide more barbs 46, and that the barbs can be arranged other than in a common plane. FIG. 11, for example, shows a marker 40A comprising three wires 41, 42, and 43, anchored within a tube 45. Three barbs are formed at each end of the marker 40A and are disposed at 120° intervals. FIG. 12 shows a marker 40B comprising four wires 41–44 anchored within a tubing 45 and forming four barbs 46 at each end of the marker which are disposed at 90° intervals.

FIG. 13 shows a marker 50 comprised of two pieces of wire 51, 52 whose middle portions are twisted together as at 55. The free ends of the wires 51, 52 are bent outward to form barbs 56.

FIG. 14 shows another marker 60 comprised of a pair of wires 61, 62 whose central portions are welded together at 65. The free ends of the wires are bent outward to form barbs 66.

In addition to securing wires within a tubing, twisting wires together, or welding wires together, it will be appreciated that other means for fastening two or more wires together along their intermediate portions can be employed, including but not limited to adhesive bonding, heat shrink tubing, or other suitable biocompatible methods. In addition, while the barbed markers previously described are all fabricated by fastening two or more wires together, it is feasible to fabricate a marker from a single piece of material, for example, an elongated strip which is split at both ends, the middle portion remaining intact while the split ends are bent to form a plurality of barbs.

FIGS. 15–17 illustrate the procedure for implanting a barbed-type marker. While the procedure will be demonstrated with respect to a marker 40 in which the wires 41, 42 are fastened together by means of a tubing 45, it will be appreciated that the same procedure is used to implant a marker 50 whose wires are twisted together, or a marker 60 whose wires are welded together.

Referring first to FIG. 15, the barbs 46 at the forward end of the marker 40 are pressed together so that the free ends fit into the rearward end of the cannula 30. The marker 40 is advanced into the cannula. As the barbs 46 at the rearward end of the marker pass into the bore of the cannula 30, contact with the walls of the cannula force the trailing barbs into a substantially straight configuration. Though not shown in FIGS. 15–17, a plurality of markers 40 can be sequentially loaded into the cannula 30, as was described above with respect to the marker 10. A stylet 32 inserted into the rearward end of the cannula 30 is used to advance the marker or markers 40 forward through the cannula and to eject the marker(s) from the forward end of the cannula. As a marker 40 exits the forward end of the cannula 30, the barbs 46 spring outward, as shown in FIG. 17, piercing the target tissue 34 and anchoring the marker to the tissue.

It will be appreciated that a plurality of markers 40, 50, or 60 can be implanted in a single insertion, as explained above with respect to FIGS. 5–8, by sequentially loading a plurality of markers into a needle. If needed, to prevent the barbs of adjacent markers from riding up over one another and becoming entangled, adjacent markers can be separated by a small plug of a biodegradable material.

FIGS. 18–21 illustrate a device 70 for implanting markers 10 according to the present invention. The implantation device 70 includes a housing 72 formed from a pair of mating housing halves (only one of which is shown in the cutaway views of FIGS. 18–21). A hollow cannula 74 having a forward end 75 is mounted to the front 76 of the housing 72. A cantilevered latch arm 77, the end of which is seen in FIGS. 18–21, projects from the interior wall of the housing 72 in a direction which is generally perpendicular to the longitudinal axis of the device 70.

A trigger **78** is pivotably mounted on a pin **80** formed on the housing **72**. A spring arm **82** is integrally molded with the trigger **78** and engages the housing **72** to bias the trigger **78** downward. Also molded integrally with the trigger **78** is an arm **84**, which is attached to the trigger at its lower end by an integral hinge **86**. The arm **84** has a free upper end **88**.

A slide **90** is mounted within the housing **72** for linear movement along the longitudinal axis of the device. A stylet **92** extends forward from the slide **90** and is telescopically received within the hollow cannula **74**. A coil spring **93** biases the slide rearward within the housing **72**. A plurality of ratchet teeth **94, 96** are formed on the lower surface of the slide **90**. The distance between the crests of adjacent ratchet teeth **94, 96** is equal to the length of a marker **10** in its uncoiled state. The upper end **88** of the arm **84** engages the ratchet teeth **94, 96** and prevents the slide **90** from moving rearward under the force of the spring **93**.

The deployment sequence by which two markers **10*a***, **10*b*** are implanted will now be explained with reference to FIGS. **18–21**. Referring first to FIG. **18**, the two markers **10*a***, **10*b*** are mounted within the forward end of the hollow cannula **74**. The shape memory of the markers **10*a***, **10*b*** causes them to assume a slightly bowed configuration, which creates sufficient friction with the interior walls of the cannula **74** to prevent the markers from sliding out of the forward end **75** of the cannula. The slide **90** is in its full rearward position, the latch arm **77** of the housing **72** resting in front of the first ratchet tooth **94**. The upper end **88** of the arm **84** engages the trailing face of the first ratchet tooth **94**.

In FIG. **19** the trigger **78** has been depressed. The rotation of the trigger **78** causes the arm **84** to move forward to advance the slide **90**. The latch arm **77** is deflected downward from its original position (shown in dashed lines **77'**) as the first ratchet tooth **94** advances over it. As the slide **90** advances, the stylet **92** pushes on the rearward marker **10*b***, which in turn pushes the front marker **10*a*** out of the forward end **75** of the cannula **74**.

In FIG. **20** the trigger **78** has been released. The spring arm **82** pivots the trigger **78** downward, retracting the arm **84**. The latch arm **77** of the housing engages the trailing edge of the front ratchet tooth **94** of the slide **90** to prevent the slide from moving rearward. The upper end **88** of the arm **84** now engages the trailing edge of the second ratchet tooth **96** of the slide **90**. As can also be seen in FIG. **20**, the first marker **10*a*** assumes its helical shape memory upon being exposed to the body temperature of the target tissue.

At this point, the instrument **70** can be repositioned to bring the forward end **75** of the cannula **74** into position adjacent a second target site. The trigger **78** is then depressed again, as shown in FIG. **21**, causing the arm **84** to advance the slide **90**. As the slide **90** advances, the stylet **92** forces the second marker **10*b*** out of the forward end **75** of the cannula **74**. The latch arm **77** is deflected downward again from its original position (shown in dashed lines **77'**) as the second ratchet tooth **96** passes. The latch arm **77** then springs upward as the second ratchet tooth **96** clears the latch arm to engage the trailing edge of the second ratchet tooth.

While the device **70** of FIGS. **18–21** is designed to implant two markers **10**, it will be appreciated that the device can easily be modified to implant a greater or lesser number of markers by providing a longer or shorter slide with a greater or lesser number of ratchet teeth.

A feature common to all of the markers hereinabove described is that, once deployed within the target tissue, all of the markers are mechanically self-anchoring within the target tissue without the need for intervention by the physician. This feature provides the advantages that the implantation procedure is simplified, and the possibility is reduced that an omission by the physician or a mechanical malfunction of the marker will result in a marker migrating from its intended location or accidentally causing injury to the patient.

Finally, it will be understood that the preferred embodiment has been disclosed by way of example, and that other modifications may occur to those skilled in the art without departing from the scope and spirit of the appended claims.

What is claimed is:

1. A marker for inserting by a physician through a lumen of a hollow needle to a target site within the tissues of a patient to facilitate locating the target site at a later time, said marker being capable of assuming an essentially linear configuration for passage through said hollow needle, and said marker comprising means for anchoring itself to said tissues of said patient without intervention by said physician, wherein said marker comprises at least two wires having central portions which are fastened together, said at least two wires each having at least two free ends forming barbs for anchoring said marker within said tissues of said patient.

2. The marker of claim **1**, wherein said marker further comprises a tubular body portion, and wherein said central portions of said at least two wires are anchored within said tubular body portion with said free ends extending from said tubular body portion to form said barbs.

3. The marker of claim **1**, wherein said central portions of said at least two wires are twisted together.

4. The marker of claim **1**, wherein said central portions of said at least two wires are bonded together.

5. The marker of claim **4**, wherein said central portions of said at least two wires are welded together.

6. The marker of claim **4**, wherein said central portions of said at least two wires are adhesively bonded together.

7. A method for implanting a plurality of markers within the tissues of a patient, comprising the steps of:

providing an elongated hollow needle in which a plurality of markers are sequentially loaded, said elongated hollow needle defining a longitudinal axis;

inserting a forward end of said elongated hollow needle into the tissues of a patient and advancing said forward end of said needle to a first target location;

discharging a first one of said plurality of markers from said forward end of said hollow needle in a direction substantially parallel to said longitudinal axis of said elongated hollow needle and into the tissues of said patient;

relocating said forward end of said hollow needle to a second target location;

discharging a second one of said plurality of markers from said forward end of said hollow needle in a direction substantially parallel to said longitudinal axis of said elongated hollow needle and into the tissues of said patient.

8. The method of claim **7**, wherein said steps of discharging said first one and said second one of said plurality of markers from said forward end of said hollow needle comprise the steps of:

advancing a stylet forward within said hollow needle to push a rearmost one of said plurality of sequentially loaded markers so as to cause said first one and said second one of said markers to be discharged from said forward end of said needle.

9. An apparatus for delivering a plurality of implants to target locations within the tissues of a patient, comprising:

a housing;

an elongated hollow cannula mounted to said housing, said cannula having a longitudinal axis, and said cannula being configured to receive said plurality of implants within a forward end thereof, each of said implants having a length when disposed within said forward end of said cannula;

a slide mounted to said housing for movement in a direction generally parallel to said longitudinal axis of said cannula, said slide having a rearmost position;

a stylet telescopically received within said cannula and having a forward end and a rearward end mounted to said slide, said stylet having a length such as will cause said forward end of said stylet to bear against a rearward portion of the rearmost of said plurality of implants when said slide is in said rearmost position;

a trigger; and

means operatively associated with said trigger and operative upon actuation of said trigger for advancing said slide and said stylet attached thereto by a distance equal to said length of each of said implants,

whereby actuation of said trigger causes a single one of said plurality of implants to be ejected from said forward end of said cannula in a direction substantially parallel to said longitudinal axis of said cannula.

10. The apparatus of claim 9, wherein said means operatively associated with said trigger for advancing said slide comprises an arm attached to said trigger which engages a plurality of ratchet teeth on said slide.

11. The apparatus of claim 10, wherein an adjacent pair of said plurality of ratchet teeth is spaced apart by a distance equal to said length of each of said implants.

* * * * *

US006425903B1

(12) **United States Patent**
Voegele

(10) **Patent No.: US 6,425,903 B1**
(45) **Date of Patent: Jul. 30, 2002**

(54) **IMPLANTABLE SURGICAL MARKER**

(76) Inventor: **James W. Voegele**, 11486 Kemperknoll Rd., Cincinnati, OH (US) 45249

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(21) Appl. No.: **09/567,211**

(22) Filed: **May 9, 2000**

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(52) **U.S. Cl.** **606/151**; 606/219; 606/220; 606/157; 606/116; 411/472

(58) **Field of Search** 606/219, 220, 606/221, 151, 157, 213, 215, 139, 143, 155, 72, 75, 116; 600/562; 128/899; 411/457, 460, 461, 463, 471, 470, 472, 475, 481, 920

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Primary Examiner—Amy B. Vanatta

(57) **ABSTRACT**

An implantable marker for implantation in tissue of a surgical patient is disclosed. The marker has a base and an elevated bridge. A pair of legs descend from first and second transitions of the bridge. Each leg has a distal tip, a generally straight leg arm adjacent the tip, a camming marker surface between the transitions of the base and the straight leg arm, and a camming marker surface notch. The camming marker surfaces extend outwardly from the straight leg arms of the legs. In its pre-formed configuration, the first and second straight leg arms of the legs of the marker are generally parallel to each other. In its open form configuration, the first and second straight leg arms initially converge towards each other, then diverge into an open form generally taking the shape of the letter "W". The marker is particularly adapted for fixation in tissue to mark the site of a lesion or other abnormal tissue which may be removed during a biopsy procedure, for example a breast biopsy procedure. Advantageously, the camming marker surfaces of the legs of the marker and the camming marker surface notches facilitate the ability to form the marker upon pushing the marker distally into the tissue, thus insuring deep penetration and anchoring of the marker securely in the tissue regardless of tissue density.

9 Claims, 3 Drawing Sheets

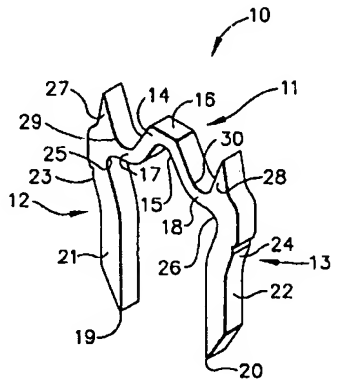

Exhibit D

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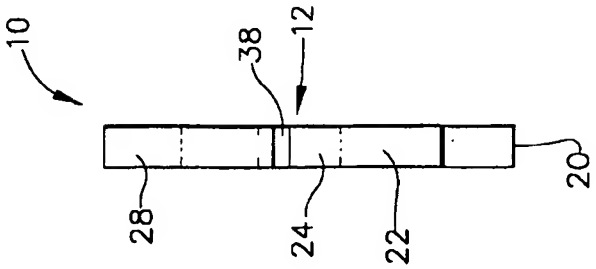


FIG. 3

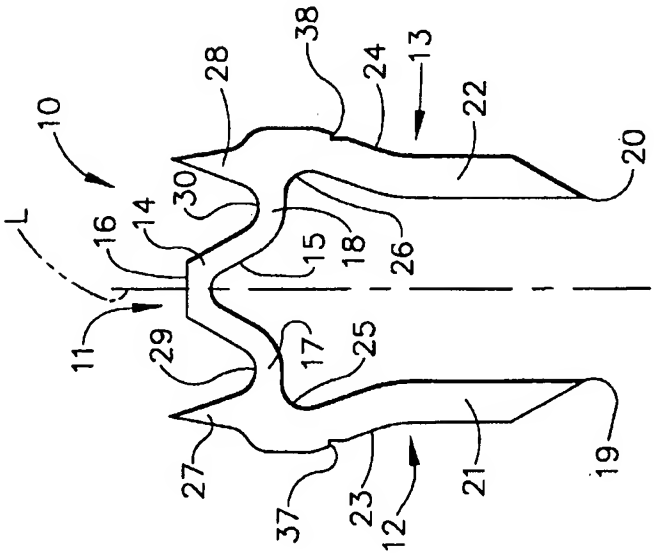


FIG. 2

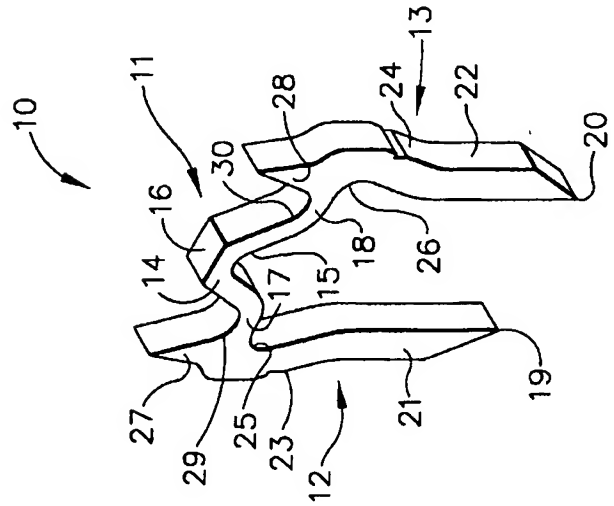


FIG. 1

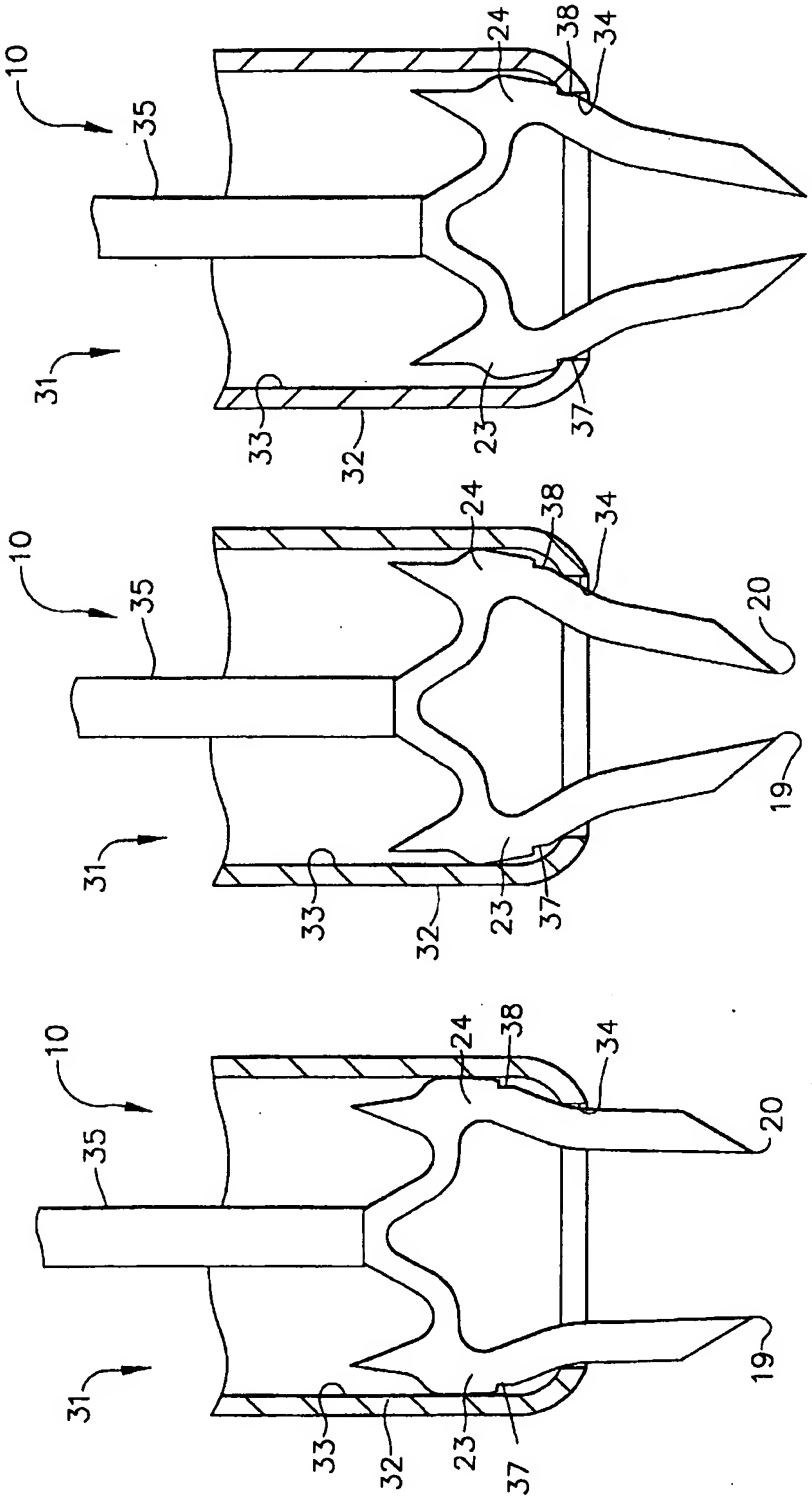


FIG. 6

FIG. 5

FIG. 4

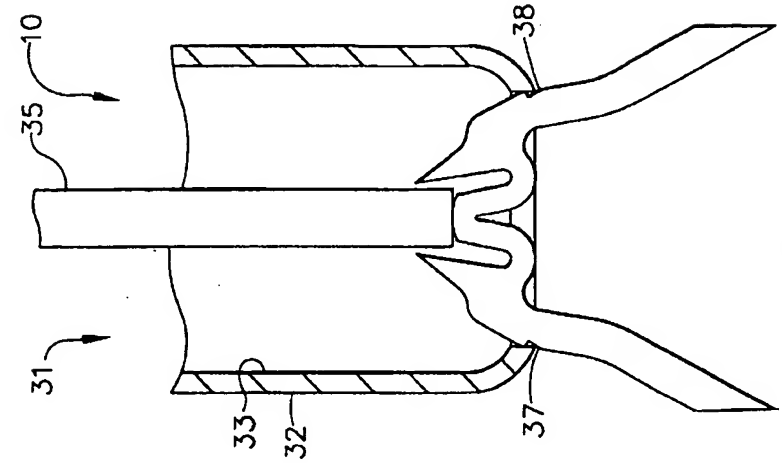


FIG. 9

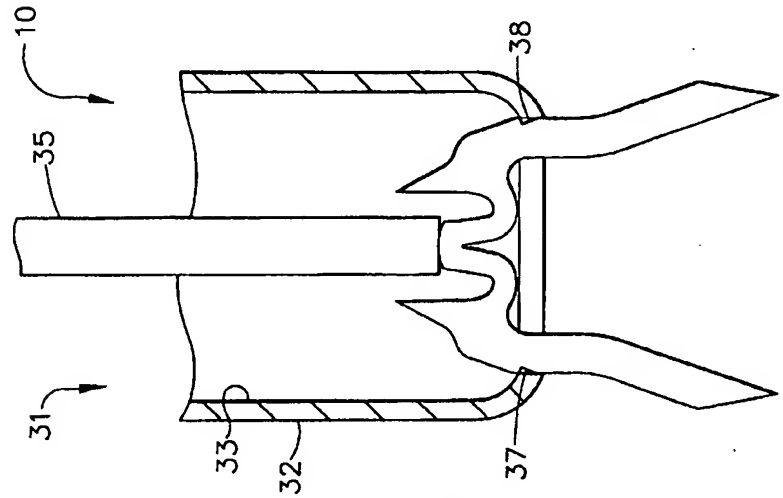


FIG. 8

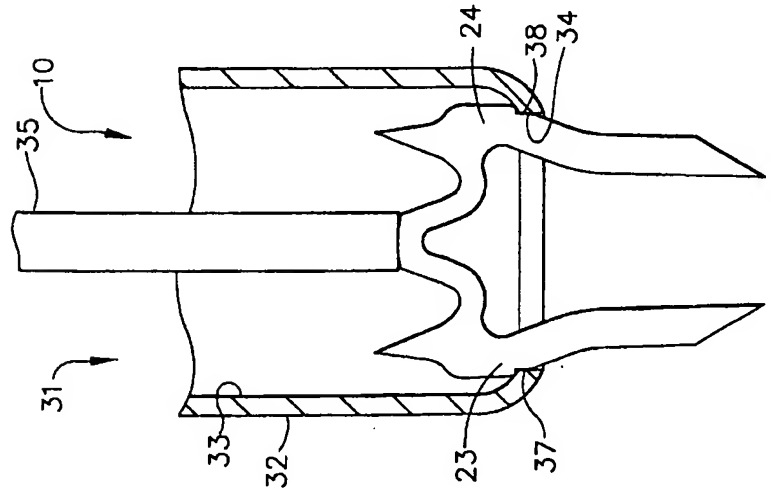


FIG. 7

IMPLANTABLE SURGICAL MARKER

BACKGROUND OF THE INVENTION

This invention relates to a marker for implantation in tissue of a surgical patent. More specifically, it relates to an implantable marker for defining particular locations in human tissue, particularly in a human breast.

One in nine American women will develop breast cancer in their lifetime. It is the leading cause of cancer deaths in women 40–55 years of age and the second leading cause of cancer deaths in women overall. Breast cancer will be diagnosed in approximately one in eight women in their lifetime, and one in 30 will die of this disease. Breast cancer does occur in males but is much less common. Biopsy requests stem from a screening process generally performed via a physical examination (palpable) and/or mammogram (non-palpable). A biopsy is indicated if suspicious tissue is detected. Five out of six biopsies performed return benign indications.

It is desirable and often necessary to perform procedures for detecting, sampling, and testing lesions and other abnormalities in the tissue of humans and other animals, particularly in the diagnosis and treatment of patients with cancerous tumors, pre-malignant condition and other diseases or disorders. Typically, in the case of cancer, when a physician establishes by means of known procedures (i.e. palpation, x-ray, MRI, or ultrasound imaging) that suspicious circumstances exist, a biopsy is performed to determine whether the cells are cancerous. Biopsy may be an open or percutaneous technique. Open biopsy removes the entire mass (excisional biopsy) or a part of the mass (incisional biopsy). Percutaneous biopsy on the other hand is usually done with a needle-like instrument and may be either a fine needle aspiration (FNA) or a core biopsy. In FNA biopsy, very small needles are used to obtain individual cells or clusters of cells for cytologic examination. The cells may be prepared such as in a Papanicolaou (Pap) smear. In core biopsy, as the term suggests, a core or fragment of tissue is obtained for histologic examination, which may be done via a frozen section or paraffin section. The chief difference between FNA and core biopsy is the size of the tissue sample taken. An imaging system having spectroscopic capabilities, such as the stereotactic guidance system described in U.S. Pat. No. 5,240,011 is employed to guide the extraction instrument to the lesion.

Depending on the procedure being performed, the sample may result in the suspicious lesion being partially or completely removed. Visibility of the lesion by the imaging system may be hampered because of the distortion created by the extraction process itself as well as associated bleeding in the surrounding tissues. Although the lesion is removed and all fluids are continuously aspirated from the extraction site, it is likely that the process will "cloud" the lesion, thus impairing exact recognition of its margins. This makes it difficult to ensure that the entire lesion will be removed.

Often, the lesion is merely a calcification derived from dead abnormal tissue, which may be cancerous or pre-cancerous, and it is desirable to remove only a sample of the lesion, rather than the entire lesion, to evaluate it. This is because such a lesion actually serves to mark or define the location of adjacent abnormal tissue, so the physician does not wish to remove the entire lesion and thereby lose a critical means for later relocating the affected tissue. One of the benefits to the patient from core biopsy is that the mass of the tissue taken is small. However, oftentimes, either inadvertently or because the lesion is too small, the entire lesion is removed for evaluation, even though it is desirable to remove only a portion. Then, if subsequent analysis indicates the tissue to be malignant (malignant tissue requires removal, days or weeks later, of tissue around the immediate site of the original biopsy), it is difficult for the physician to determine the precise location of the lesion, in order to perform necessary additional procedures on adjacent potentially cancerous tissue. Additionally, even if the lesion is found to be benign, there will be no evidence of its location during future examinations, to mark the location of the previously removed calcification so that the affected tissue may be carefully monitored for future reoccurrence.

Thus, it would be of considerable benefit to be able to permanently mark the location or margins of such a lesion prior to or immediately after removing the sample. Marking prior to removal would help to ensure that the entire lesion is excised, if desired. Alternatively, if the lesion were inadvertently removed in its entirety, marking the biopsy site immediately after the procedure would enable re-establishment of its location for future identification.

A number of procedures and devices for marking and locating particular tissue locations are known in the prior art. For example, location wire guides, such as that described in U.S. Pat. No. 5,221,269 to Miller et al, are well known for locating lesions, particularly in the breast. The device described by Miller comprises a tubular introducer needle and an attached wire guide, which has at its distal end a helical coil configuration for locking into position about the targeted lesion. The needle is introduced onto the breast and guided to the lesion site using an imaging system of a known type, for example, x-ray, ultrasound or magnetic resonance imaging (MRI), at which time the helical coil at the distal end is deployed about the lesion. Then, the needle may be removed from the wire guide, which remains in a locked position distally about the lesion for guiding a surgeon down the wire to the lesion site during subsequent surgery. While such a location system is effective, it is obviously intended and designed to be only temporary, and is removed once the surgery or other procedure has been completed.

Other devices are known for marking external regions of a patient's skin. For example, U.S. Pat. No. 5,192,270 to Carswell, Jr. discloses a syringe which dispenses a colorant to give a visual indication on the surface of the point at which an injection has or will be given. Similarly, U.S. Pat. No. 5,147,307 to Gluck discloses a device which has patterning elements for impressing a temporary mark in a patients skin, for guiding the location of an injection or the like. It is also known to tape or otherwise adhere a small metallic marker, e.g. a 3 millimeter diameter lead sphere, on the skin of a human breast in order to delineate the location of skin calcifications (see Homer et al, The Geographic Cluster of Microcalcifications of the Breast, Surgery, Gynecology, & Obstetrics, December 1985). Obviously, however, none of these approaches are useful for marking and delineating internal tissue abnormalities, such as lesions or tumors.

Still another approach for marking potential lesions and tumors of the breast is described in U.S. Pat. No. 4,080,959. In the described procedure, the skin of the portion of the body to be evaluated, such as the breasts, is coated with a heat sensitive color-responsive chemical, after which that portion of the body is heated with penetrating radiation such as diathermy. Then, the coated body portion is scanned for color changes which would indicate hot spots beneath the skin surface. These so-called hot spots may represent a tumor or lesion, which does not dissipate heat as rapidly because of its relatively poor blood circulation (about 1/20 of

the blood flow through normal body tissue). This method, of course, functions as a temporary diagnostic tool, rather than in a permanent means for delineating the location of a tumor or lesion.

A method of identifying and treating abnormal neoplastic tissue or pathogens within the body is described in U.S. Pat. No. 4,649,151 to Doughety et al. In this method, a tumor-selective photosensitizing drug is introduced into a patient's body, where it is cleared from normal tissue faster than it is cleared from abnormal tissue. After the drug clears normal tissue but before it has cleared abnormal neoplastic tissue, the abnormal neoplastic tissue may be located by the luminescence of the drug within the abnormal tissue. The fluorescence may be observed with low intensity light, some of which is within the drug's absorbency spectrum. Once detected, the tissue may be destroyed by further application of higher intensity light having a frequency within the absorbency spectrum of the drug. Of course, this method also is only a temporary means for marking the abnormal tissue. Additionally, once the abnormal tissue has been destroyed during treatment, the marker is destroyed as well.

It is also known to employ biocompatible dyes or stains to mark breast lesions. First, a syringe containing the colorant is guided to a detected lesion, using an imaging system. Later, during the extraction procedure, the surgeon harvests a tissue sample from the stained tissue. However, while such staining techniques can be effective, it is difficult to precisely localize the stain. Also, the stains are difficult to detect flouoroscopically and may not always be permanent.

Additionally, it is known to implant markers directly into a patient's body using invasive surgical techniques. For example, during a coronary artery bypass graft (CABG), which of course constitutes open-heart surgery, it is common practice to surgically apply one or more metallic rings to the aorta at the site of the graft. This enables a practitioner to later return to the site of the graft by identifying the rings, for evaluative purposes. It is also common practice to mark a surgical site with staples, vascular clips, and the like, for the purpose of future evaluation of the site.

A technique has been described for the study of pharyngeal swallowing in dogs, which involves permanently implanting steel marker beads in the submucosa of the pharynx (S. S. Kramer et al, A Permanent Radiopaque Marker Technique for the Study of Pharyngeal Swallowing of Dogs, Dysphagia, Vol. 1, pp.163–167, 1987). The article posits that the radiographic study of these marker beads during swallowing on many occasions over a substantial period of time provides a better understanding of the pharyngeal phase of deglutition on humans. In the described technique, the beads were deposited using a metallic needle cannula having an internal diameter slightly smaller than the beads to be implanted. When suction was applied to the cannula, the bead sat firmly on the tip. Once the ball-tipped cannula was inserted through tissue, the suction was broken, thereby releasing the bead, and the cannula is withdrawn.

Of course, this technique was not adapted or intended to mark specific tissue sites, but rather to mark an entire region or structure of the body in order to evaluate anatomical movements (i.e. swallowing motions). It also was not intended for use in humans.

Accordingly, what is needed is a method and device for non-surgically implanting potentially permanent markers at the site of a lesion or other abnormal tissue, for the purpose of defining the margins of a lesion before it is removed and/or to establish its location after it has been removed. The markers should be easy to deploy and easily detected using state of the art imaging techniques.

A method of implanting markers directly into a patient's body using minimally invasive surgical techniques is described in International Patent No. WO 9608208A1 to Foerster et al. In this method, a clipping device is introduced to the lesion site by a tubular cannula. Once the clip is at the lesion site, an actuating means at the proximal end outside the patient deploys the clip into the tissue. This marking means can be used long term and can be imaged by most imaging techniques. However, because of its small size, current ultrasound imaging systems are unable to detect it within the tissue.

Another method of implanting a marker is described in U.S. Pat. No. 5,902,310 to Foerster et al. The marker described in this method utilizes a central tang that is tensily loaded to cause a squarely supported, end contact bridge on the marker to bend resulting in the goal post arms to swing inward in an arcuate fashion to pinch tissue. The tensile load on the tang is increased until it breaks at a predetermined location leaving the marker attached to the tissue site. Unfortunately, this method requires the marker to be pulled away from tissue when the marker is formed, consequently, limiting marker penetration and the amount of tissue grasped.

A surgical clip for permanently joining opposed tissue for an anastomosis procedure is described in U.S. Pat. No. 4,733,664 to Kirsh et al. This is accomplished using an applier, also disclosed, to pull on a frangible central tang to close a pair of spaced arcuate arms extending generally parallel in one direction from opposite ends of the plastically deformable bridge. The arms are brought around opposed tissue. A predetermined force is applied to create a tensile break of the neck in the tang. Specific angles of clip shoulder and applier are given. The applier jaw faces are in the range of 120° to 180° with respect to one another, specifically 150° Unfortunately, the method of forming this clip suffers a fate similar to the method described in the preceding paragraph.

U.S. Pat. No. 5,941,890 to Voegele et al describes an implantable marker for implantation into a surgical patient. The marker is described as comprising a base, and first and second legs extending from the base. The base of the marker includes an elevated bridge. The first and second legs are generally straight and generally parallel to each other in the marker's pre-formed condition. Each leg includes a camming surface on its exterior wall. The appearance of the marker, in its pre-formed condition, is similar to the letter "U".

To administer the marker described in the '890 patent, an applier is used. The applier includes a push rod and tube with a camming wall surface at its distal end. The push rod functions to contact the elevated bridge of the marker and push the marker from the applier into the targeted tissue. As the marker is pushed, the camming surface on each leg of the marker is cammed against the camming wall surface of the applier. This interaction causes the distal tips of the marker legs to converge towards each other as the elevated bridge deforms, causing the targeted tissue to become entrapped between the legs. The marker is fully formed essentially when the distal tips of the legs touch, the formed marker now generally diamond shaped. As the push rod continues to apply force to the elevated bridge, the marker exits the distal end of the applier. The benefits of this marker are described as its ability to be pushed into tissue for deeper penetration and an ability to "grasp" a greater amount of tissue in contrast to conventional markers.

The deeper penetration is indeed a great attribute, however, the depth of penetration is largely determined by

the composition and density of the tissue to which the marker is applied. The breast, for example, is made up of a wide range of densities of tissue, from very soft, fatty tissue to very firm and dense muscular tissue. The marker described may indeed penetrate and grasp very soft, fatty tissue, however the structure of the tissue may be such that the marker would easily tear away from the tissue, leaving the marker to move and migrate within the breast, obviously an undesirable condition. Similarly if the tissue involved is extremely dense, i.e. muscular, the marker may meet resistance to forming into its final "diamond" shape. As a result, the marker may not be securely attached to the tissue and again may become dislodged.

Furthermore, the marker described, in its final diamond formation, is relatively small and compact in size. This attribute may make the marker more difficult to identify on x-ray images or images from other known imaging modalities previously described.

Accordingly, what is needed is a surgical marker for implantation at the sites of a lesion or other abnormal tissue, for the purpose of defining the margins of a lesion before it is removed or to establish its location after it has been removed. The marker should be easy to deploy and more easily detected using state of the art imaging techniques. Additionally, the marker must be capable of being securely anchored into a wide range of tissue densities without risk of becoming dislodged.

SUMMARY OF THE INVENTION

The invention is an implantable marker for implantation in tissue of a surgical patient. The marker comprises a base, and first and second legs.

The base of the marker includes an elevated bridge. The bridge has a top and a pair of top arcuate surfaces separated by the top. The bridge is bounded by first and second transitions.

The first leg descends from the first transition of the base. The first leg includes the following: a) a first distal tip remote from the first transition, b) a generally straight first leg arm adjacent the first distal tip, and c) a first camming marker surface between the first transition of the base and the first straight leg arm. The first camming marker surface extends outwardly from the first straight leg arm.

The second leg of the marker descends from the second transition of the base. The second leg includes the following: a) a second distal tip remote from the first transition, b) a generally straight second leg arm adjacent the second distal tip, and c) a second camming marker surface between the second transition of the base and the second straight leg arm. The second camming marker surface extends outwardly from the straight second leg arm. A first camming marker surface notch is located on the first camming marker surface. A second camming marker surface notch is located on the second camming marker surface.

The first and second straight leg arms are generally parallel to each other when the marker is in a pre-formed configuration. The first and second straight leg arms initially converge towards each other from a spaced-apart position adjacent the first and second transitions and then diverge into an open form configuration so that the distal tips of the legs are separated from each other.

Significantly, the first and second camming marker surface notches on the camming marker surfaces of the legs of the marker of this invention facilitate the deployment of the marker in a manner in which the marker can be pushed into the tissue during deployment for deep tissue penetration regardless of the particular tissue characteristics. This is so because as the legs initially converge and then diverge, the marker is securely anchored in the tissue notwithstanding whether the tissue is soft and fatty or dense and muscular. In addition, and in contrast to the prior art markers,the marker of this invention is less likely to unintentionally dislodge because of its enhqanced anchoring ability in its open form configuration. Furthermore, the final open form configuration of the marker also contributes to its ability to be more easily identified on x-ray images or images from other known imaging modalities.

The marker of this invention is especially adapted for implantation at the site of a lesion or other abnormal tissue particularly during a biopsy procedure to define the margins of a lesion before it is biopsied or to establish its location at some later time after the biopsy sample has been removed.

BRIEF DESCRIPTION OF THE DRAWINGS

FIG. **1** is an isometric view of the implantable marker constructed in accordance with a preferred embodiment of this invention.

FIG. **2** is a front elevational view of the marker of FIG. **1**.

FIG. **3** is a side elevational view of the marker of FIG. **1**.

FIG. **4** is a fragmentary distal end sectional view illustrating the plan view of the marker of FIG. **1** in its loaded position within the shaft of an applier.

FIGS. **5–9** are fragmentary distal end sectional views illustrating sequentially the formation of the loaded marker depicted in FIG. **4**.

DETAILED DESCRIPTION OF THE PREFERRED EMBODIMENT

Referring initially to FIGS. **1–3**, the preferred marker **10** of this invention is illustrated. The marker has a base **11** and first and second legs, **12** and **13**, respectively. The base has an elevated bridge **14**. The elevated bridge has an arcuate bottom surface **15**. It also has a generally flat top **16**.

The marker has a first transition **17** on one side of the elevated bridge and a second transition **18** on the other side of the elevated bridge. The first and second transitions separate the elevated bridge of the base from the descending first and second legs of the marker. The first leg has a first, beveled pointed tip **19** at the distal end of the leg remote from the first transition **17**. Similarly, the second leg has a second, beveled pointed tip **20** at its distal end. Adjacent the first and second pointed tips of the legs, there are first and second straight leg arms, **21** and **22**, respectively. Interposed between the first and second transitions and the first and second straight leg arms, are first and second camming marker surfaces **23** and **24**, respectively. The camming marker surfaces extend outwardly from the straight leg arms of the legs. The first and second camming marker surfaces have first and second interior surfaces, **25** and **26**, respectively, which are arcuate in configuration.

The marker has first and second reverse cleats, **27** and **28**, respectively. The cleats are triangular in configuration. The first cleat protrudes from the first camming marker surface and the first transition. Similarly, the second cleat protrudes from the second camming marker surface and the second transition. The cleats protrude generally parallel to the first and second straight leg arms of the legs.

The marker has first and second camming marker surface notches, **37** and **38**, respectively. The notches are generally V-shaped indentations in the camming surfaces. The first camming marker surface notch **37** is located on first cam-

ming marker surface **23** below first reverse cleat **27**. Similarly, the second camming marker surface notch **38** is located on second camming marker surface **24** below second reverse cleat **28**.

The bridge of the marker has a pair of top arcuate surfaces, **29** and **30**, respectively, separated by the flat top of the bridge on the base of the marker. The first top arcuate surface **29** is bounded by the interior surface of the first spike and the surface adjacent the flat top of the elevated bridge. In a similar fashion, the second top arcuate surface **30** is bounded by the interior surface of the second spike and the surface adjacent the flat top.

The preferred marker is symmetrical about a centerline axis taken through the center of the elevated bridge **14** of the base of the marker, and drawn parallel to the first and second straight leg arms, **21** and **22**, of the legs. The centerline axis is designated as "L" in FIG. **2**. In addition, the region of the marker between the flat top of the elevated bridge and the arcuate bottom surface of the bridge can be characterized as a bridge flexure region of reduced thickness. The flexure region of the elevated bridge increases the flexibility of the marker when it is deployed from its pre-formed position to its open formed position. This increased flexibility, coupled with the arcuate symmetrical nature of the elevated bridge, provides a uniform load on the base of the marker during marker formation. In its pre-formed configuration, the first and second straight leg arms of the legs of the marker are generally parallel to each other.

The first and second reverse cleats of the marker are provided to prevent undesired migration of the formed marker when it is in its final open form configuration in tissue by preventing tissue from sliding off of the bridge. Consequently, the surface of the bridge firmly bears against tissue to prevent undesired migration of the marker.

Referring now to FIGS. **4–9**, there is illustrated the deployment of the preferred marker of this invention from its pre-form configuration to its open form configuration. A marker applier **31** is provided which has a tubular shaft **32**. The marker **10** is positioned inside the tubular shaft. The tubular shaft is sized so that the camming marker surfaces **23** and **24** of the legs of the marker contact the shaft inner wall **33** of the tubular shaft. The distal end of the tubular shaft has a distal camming wall surface **34** extending radially inwardly from the shaft inner-wall. The distal camming wall surface is sized so that this surface contacts the first and second straight leg arms of the legs of the marker when the marker is in its pre-form configuration, and the leg arms are parallel to each other as illustrated in FIG. **4**. An applier push rod **35** is positioned on the flat top of the elevated bridge on the base of the marker, and the pointed distal tips of the legs protrude from the tubular shaft of the applier.

When the applier push rod **35** is pushed distally to deploy the marker from its pre-form position where the straight leg arms are parallel to each other to its open form position, the marker is urged out of the tubular shaft of the applier. As the marker moves distally within the tubular shaft of the applier, the camming marker surfaces of the legs of the marker are cammed against the distal camming wall surface of the applier. This camming action urges the straight leg arms of the legs of the marker to converge towards each other as the elevated bridge of the base of the marker bends inwardly at the bridge flexure region. As the camming marker surfaces of the legs slide against the distal camming wall surface of the applier, the distal camming wall surface of the applier eventually contacts the camming marker notch in each leg. At this point the convergence of the straight leg arms ceases and the straight leg arms begin to diverge as they pivot about the camming marker surface notch. They continue to pivot and diverge until the camming marker surface notch is forced past the distal camming wall surface of the applier. The applier push rod continues to apply force to the elevated bridge of the marker until the marker exits the distal end of the applier. The marker has formed a generally "W" shaped configuration as depicted in FIG. **9**

The preferred applier for delivering and deploying the marker of this invention is described in detail in commonly assigned, copending application Ser. No. 09/105,570, filed Jun. 26, 1998

The marker of this invention can be made of any implantable material which is biocompatible and can exhibit the requisite motion and force to prevent inadvertent dislodgment of the marker when it is anchored in tissue. The preferred marker of this invention is composed of 316 LVM stainless steel (316 L stainless steel fabricated in a vacuum melt furnace for higher purity). Alternatively, the marker may be composed of absorbable polymers, as well as non-magnetic materials particularly suited for MRI imaging applications.

The marker can be advantageously mass produced using a conventional photoetching process to create a plurality of markers affixed to the desired carriers, typically a sheet of metal composed of 316 LVM stainless steel. The metal sheet can be cut into carrier rows, and sequentially fed into a cutting die for shearing the individual markers from the carrier rows.

The marker of this invention can be coated with agents to lower friction, stop bleeding or accomplish any other desired effect. Additionally the legs of the marker can be modified to include the addition of barb-like features that could increase the holding strength, migration resistance and imaging ability of the marker.

Although this invention has been described in connection with its most preferred embodiment, additional embodiments are within the scope and spirit of the claimed invention. The preferred marker of this invention is intended merely to illustrate the invention, and not limit the scope of the invention as it is defined in the claims which follow.

What is claimed is:

1. An implantable marker for implantation in tissue of a surgical patient, said marker comprising:

a) a base, said base including an elevated bridge having a top and a pair of top arcuate surfaces separated by said top, said bridge bounded by first and second transitions;

b) a first leg descending from said first transition of said base, said first leg including:

i) a first distal tip remote from said first transition;

ii) a generally straight first leg arm adjacent said first distal tip; and

iii) a first camming marker surface between said first transition of said base and said first straight leg arm, said first camming marker surface extending outwardly from said first straight leg arm;

c) a second leg descending from said second transition of said base, said second leg including:

i) a second distal tip remote from said second transition;

ii) a generally straight second leg arm adjacent said second distal tip; and

iii) a second camming marker surface between said second transition of said base and said second straight leg arm, said second camming marker surface extending outwardly from said second straight leg arm;

d) a first camming marker surface notch located on said first camming marker surface, and a second camming marker surface notch located on said second camming marker surface;

wherein said first and second straight leg arms are generally parallel to each other when said marker is in a pre-formed configuration, and said first and second straight leg arms initially converge towards each other from a spaced-apart position adjacent said first and second transitions and then diverge into an open form configuration so that the distal tips of said legs are separated from each other.

2. The implantable marker of claim 1 wherein said marker is symmetrical about a centerline axis drawn parallel to said first and second straight leg arms and taken through the center of said elevated bridge of said base of said marker.

3. The implantable marker of claim 2 wherein said marker has a "W"-shaped configuration in the open form configuration.

4. The implantable marker of claim 3 wherein said first and second distal tips of said legs are beveled pointed tips.

5. The implantable marker of claim 4 wherein said elevated bridge has an arcuate bottom surface.

6. The implantable marker of claim 5 wherein said elevated bridge has a generally flat top, and said bridge includes a bridge flexure region of reduced thickness between said flat top and said arcuate bottom surface of said elevated bridge.

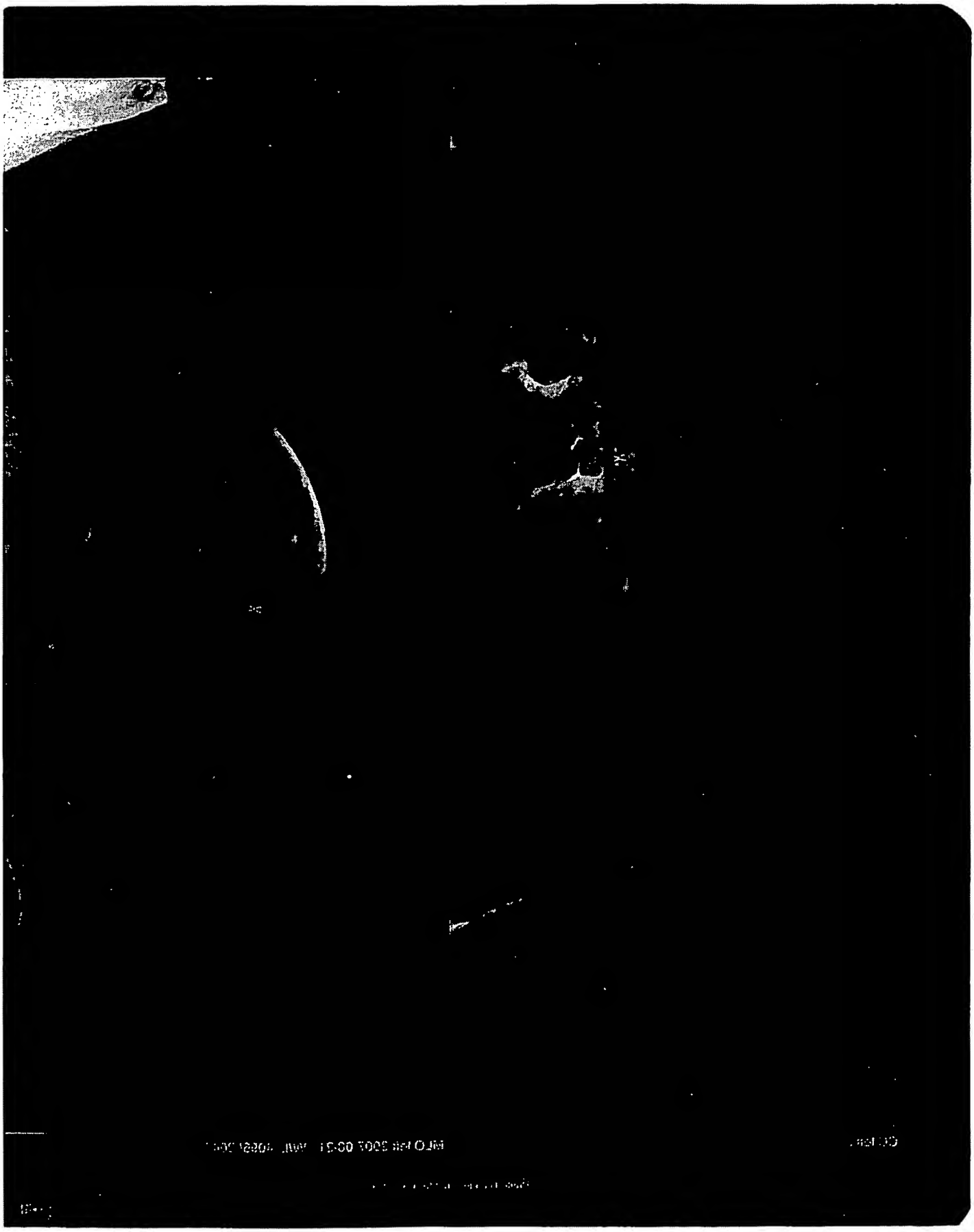
7. The implantable marker of claim 1 further comprising a first reverse cleat protruding from said first camming marker surface and said first transition, and a second reverse cleat protruding from said second camming marker surface and said second transition.

8. The implantable marker of claim 7 wherein said first and second reverse cleats are generally triangular in configuration.

9. The implantable marker of claim 8 wherein said first and second reverse cleats protrude generally parallel to said first and second straight leg arms of said legs.

* * * * *

Exhibit E



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Clip migration in stereotactic biopsy

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Abstract

Background: Needle localization breast biopsy (NLBB) is the standard for removal of breast lesions after vacuum assisted core biopsy (VACB). Disadvantages include a miss rate of 0% to 22%, a positive margin rate of approximately 50%, and vasovagal reactions (approximately 20%). We hypothesized that clip migration after VACB is clinically significant and may contribute to the positive margin rates seen after NLBB.

Methods: We performed a retrospective review of postbiopsy films in patients who had undergone VACB with stereotactic clip placement for abnormal mammograms. We measured the distance between the clip and the biopsy site in standard two view mammograms. The location of the biopsy air pocket was confirmed using the prebiopsy calcification site. The Pythagorean Theorem was used to calculate the distance the clip moved within the breast. Pathology reports on NLBB or intraoperative hematoma-directed ultrasound-guided breast biopsy (HUG, which localizes by US the VACB site) were reviewed to assess margin status.

Results: In all, 165 postbiopsy mammograms on patients who had VACB with clip placement were reviewed. In 93 evaluable cases, the mean distance the clip moved was 13.5 mm ± 1.6 mm, SEM (95% CI = 10.3 mm to 16.7 mm). Range of migration was 0 to 78.3 mm. The median was 9.5 mm. In 21.5% of patients the clip was more than 20 mm from the targeted site. Migration of the clip did not change with the age of the patient, the size of the breast or location within the breast. In the subgroup of patients with cancer, margin positivity (including those with close margins) after NLBB was 60% versus 0% in the HUG group.

Conclusions: Significant clip migration after VACB may contribute to the high positive margin status of standard NLBBs. Surgeons cannot rely on needle localization of the clip alone and must be cognizant of potential clip migration. HUG as an alternative biopsy technique after VACB eliminates operator dependency on clip location and may have superior results in margin status.

Keywords: Core needle biopsy; Stereotaxis; Breast lesions; Clip placement

More than one million breast biopsies are performed per year in the United States [1], with an increasing number of these biopsies indicated for nonpalpable mammographic abnormalities. Prior to 1990, needle localization excisional breast biopsy (NLBB) was the only means of targeting mammographic abnormalities. Percutaneous stereotactic core needle breast biopsy (SCNBB), first introduced by Parker [2] in 1990, is an accurate and less invasive alternative that is less costly than NLBB and provides a better rate of margin clearance when the diagnosis of cancer has been established prior to definitive procedure. This has influenced many surgeons in favor of SCNBB [3–7]. However, with increasing use of the vacuum-assisted core biopsy (VACB) device for SCNBB, all radiographic evidence of

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Exhibit F

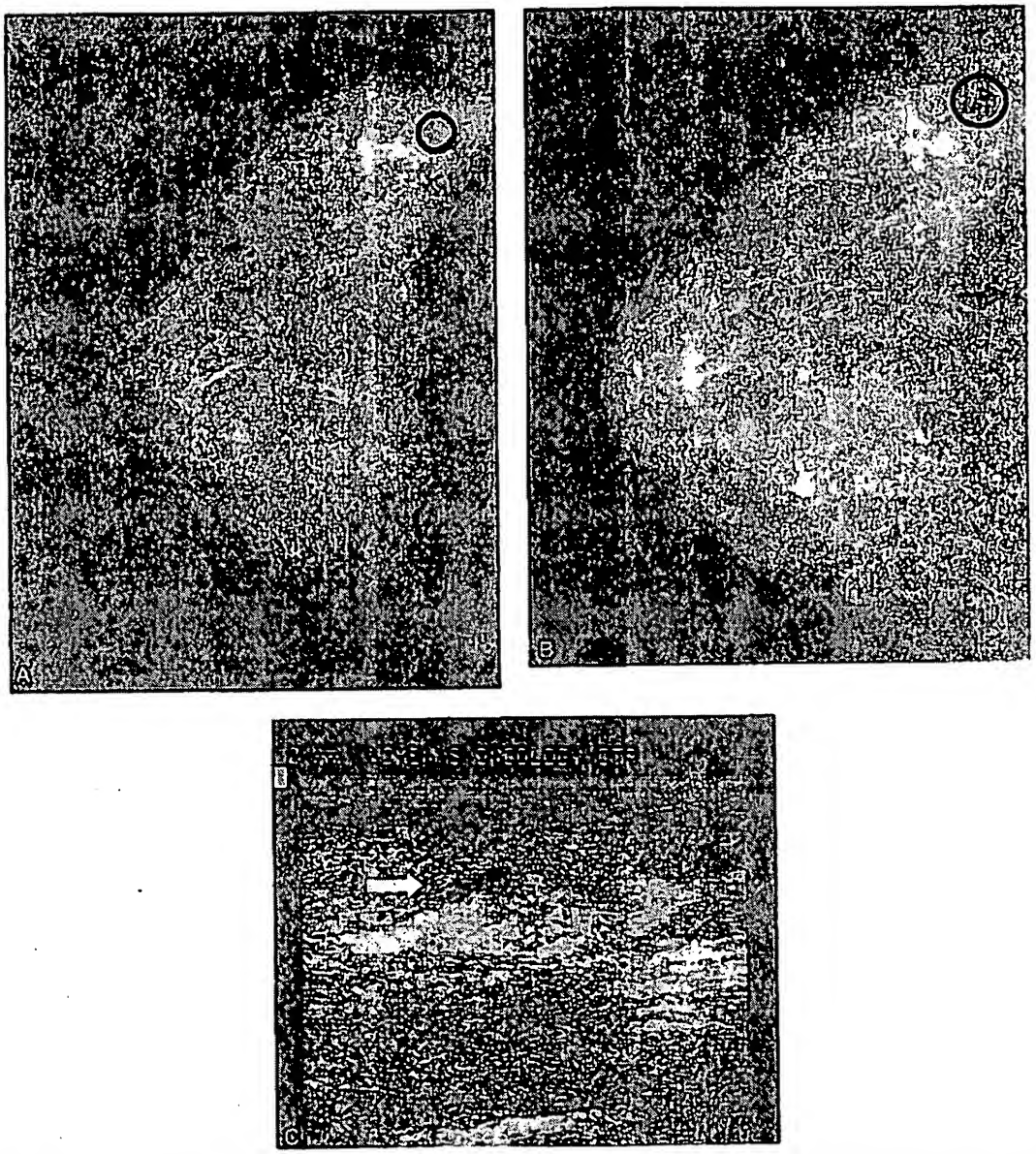

Fig. 1. (A) Encircled microcalcifications of a 49-year-old woman, as seen in the right cranial caudal view. (B) Clip (**black arrow**) migration from the biopsy site air pocket (**black circle**), after a vacuum-assisted core biopsy. Core pathology revealed ductal carcinoma in-situ (DCIS), but subsequent needle localization on the clip failed to reveal evidence of the biopsy site. (C) Intraoperative ultrasound localization of biopsy site and needle tract hematoma (white arrow) guided excisional biopsy and allowed for pathological confirmation of biopsy site. No further evidence of DCIS was seen.

lesions are frequently removed [8,9], leading to the common practice of a stereotactic clip placement in the biopsy site at the time of SCNBB. When the results of SCNBB require further evaluation, NLBB that re-targets the biopsy site based on clip location has been the traditionally method for excisional biopsy. A potential caveat of this practice is that inaccuracies in technique or migration of the clip after placement may lead to localization errors requiring further surgery for positive margins or missed lesions, as exemplified in Fig. 1.

We hypothesized that clip migration after SCNBB is clinically significant and may contribute to positive margin rates seen after NLBB. This retrospective review examines clip migration and offers intraoperative hematoma-directed ultrasound-guided breast biopsy (HUG) as an alternative localization technique that is clip independent.

Methods

Patients

Postbiopsy films of patients with abnormal mammograms who had undergone a VACB (a form of SCNBB), with clip placement were included in this study. From October 1998 through August 2001 all available films were retrospectively reviewed. The protocol for data collection was approved by the institutional review board. Inclusion criteria included ability to either visualize both clip and biopsy site on the standard two view mammograms postprocedure or ability to compare postprocedure films with preprocedure films in the same mediolateral or mediolateral oblique angle. An estimation of relative breast area was calculated for each evaluable case. This was performed by multiplication of craniocaudal and mediolateral diameters.

Stereotactic procedure

Stereotactic procedures were performed at the Arkansas Cancer Research Center by radiologists or members of the breast surgery team. VACB was performed on patients in the prone position on a dedicated stereotactic table (Mammotest; Fisher Imaging, Denver, Colorado) using an 11-gauge vacuum assisted Mammotome device (Biopsys Medical, Irving, California). After tissue removal, from October 1998 through July 15, 2001, in accordance with the mammotome instruction package, the stereotactic probe was pulled back 5 mm from biopsy position. A 2 mm clip (Micromark II; Ethicon Endo-Surgery, Cincinnati, OH) was then deployed through the probe into the biopsy site. Six month follow-up films were used to compare clip placement with biopsy site. Concern that the clip may not be attaching to the biopsy site led to a modification in clip deployment. Starting July 16, 2001, the biopsy probe was no longer pulled back 5 mm from the biopsy site prior to clip deployment. In addition, a standard two-view postprocedural mammogram was obtained after VACB.

Calculation of clip migration

Three-dimensional assessment of clip migration distance was calculated as shown in Fig. 2. In brief, the Pythagorean Theorem was applied to the series of two adjoining right triangles created using both the craniocaudal and mediolateral views. The adjoining side is the hypotenuse of both triangles and represents the true distance or migration of the clip from the biopsy site. The true distance was calculated twice, using two sets of adjoining right triangles, and then averaged. For cases of mediolateral oblique view, corrections for the degree off the perpendicular were geometrically adjusted for by using the cosine function. For these cases, the true distance was calculated based on the one available set of adjoining right triangles.

Surgical procedure

Lesions that revealed a pathological diagnosis of cancer, a risk of associated carcinoma (atypia), or that were discordantly benign with a suspicious mammogram were surgically excised either by mastectomy, NLBB or HUG as described by Smith et al [10] that localizes the core biopsy site based on the hematoma created by the stereotactic VACB procedure. Briefly, the hematoma is localized in the standard longitudinal planes and transverse planes. Dissection is then carried down toward the chest wall using a "line of site" technique [11]. Tissue is then excised around the hematoma in a block fashion to achieve a 1-cm margin. Excision of the targeted lesion was confirmed by direct visualization of the hematoma in the gross specimen as well as microscopically.

Pathology

Specimen margins were inked with six different colors for the six margins. Slides were stained with hematoxylin and eosin (H&E) and examined for evidence of malignancy. The specimen was serially sectioned at 5-mm intervals. Permanent margins were classified as positive if tumor cells were present at the inked margin, close if the lesion was less than 2 mm of the margin, and negative if the lesion was 2 mm or greater from the margin.

Statistics

The effects of age, clip location, breast size and stereotactic technique on clip migration distance were examined using correlation analysis, Cochran-Mantel Haenszel methods, and the Kruskal-Wallis Test.

Results

Patients

A total of 165 postbiopsy mammograms done on 160 patients (5 patients had bilateral procedures) who had VACB with clip placement were reviewed. The age of patients ranged from 34 to 93 years old with a mean age of 58 ± 0.9 SEM. Ninety-three films done on 91 patients met the inclusion criteria. Seventy-five of the evaluable VACB films were performed from October 1998 through July 15, 2001, the remainder (18), were performed after this date. In evaluable cases, the most frequent location (42 of 93) of lesions was the upper outer quadrant of the breast.

Stereotactic biopsy pathology

All 165 VACB specimens were sent to pathology for permanent H&E sections. Slides were reviewed at a weekly multidisciplinary breast conference with a single pathologist

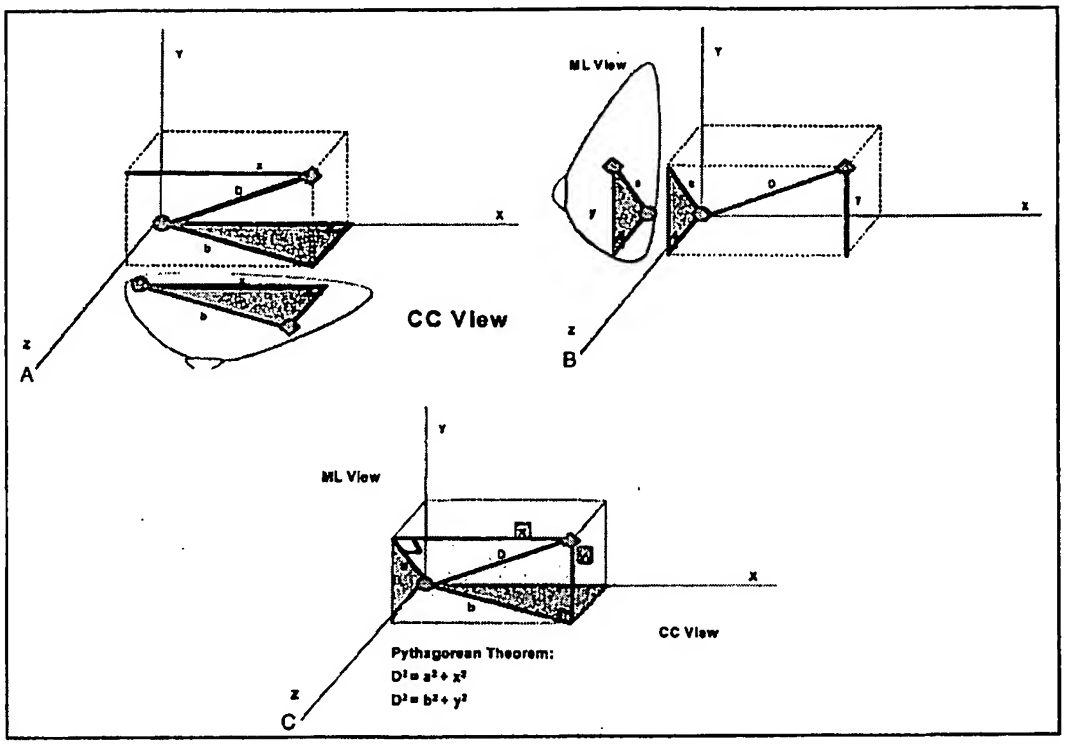

Fig. 2. (A) Relationship of biopsy site (**circle**) and clip location (**diamond**) and the distance between the two (line D), as depicted in three dimensions provided by the X, Y, and Z axis. In the forefront or XZ plane, is projection of the line D onto the cranial caudal (CC) view (line b). Note that line b is shorter than line D because it lacks depth. Line b is the hypotenuse of the right triangle that can be drawn in the CC view. Line "x" is the distance in the x axis that the clip moves on CC view and corresponds to same distance on the main rectangle in the figure. (B) Line D projects onto the mediolateral view as line "a." The right triangle drawn in the ML view provides the "y" distance that corresponds to the same distance in the main rectangle. (C) The **shaded triangles** from corresponding CC and ML views provide the distances for two more right triangles, "byD" and "axD. " which share as their hypotenuse the line D. By the principle of the Pythagorean Theorem (the hypotenuse squared equals the sum of the squares of the triangle's legs), D, or the true distance in space that the clip travels, is calculated. The calculation can by performed using either formula listed and then averaged for improved accuracy.

(SK). VACB pathology indicated that 53 specimens from 52 patients (1 patient had bilateral specimens) would require surgical excision. Eight patients had infiltrating mammary carcinoma and 14 patients had ductal carcinoma in situ (DCIS). VACB showed the remaining patients requiring reexcision had lobular carcinoma in situ (LCIS)(1), atypical ductal hyperplasia (6), atypical lobular hyperplasia (4), papillomas (9), radial scar (2), fibroadenoma with atypia (1) and discordant pathology with mammographic findings (8). Ten of the 52 patients declined further surgical work-up. All ten patients had lesions that were associated with a higher risk for carcinoma but not frank cancer.

Clip migration

In the 93 evaluable cases, the mean distance that the clip moved was 13.5 mm ± 1.6 mm (95% CI = 10.3 mm to 16.7 mm). The range of migration was 0 to 78.3 mm. The median was 9.5 mm with lower and upper quartiles of 3.0 mm and 16.4 mm, respectively. The mode was 0 mm. Fig. 3 depicts the frequency distribution. In 21.5% of patients the clip was more than 20 mm from the targeted site. There was no significant difference in migration distances for procedures done prior to July 16, 2001 compared with those done at a later date. Migration of the clip did not change with size of the breast, location within the breast, or patient age.

Surgical procedure

Of 160 patients, 42 underwent surgical reexcision of VACB site for core pathology findings (43 specimens). There were a total of 9 mastectomies, 15 NLBBs, 18 HUGs, based on VACB hematoma localization. One additional specimen was excised using a combination of NLBB and HUG. In the subgroup that had cancer (23 of 43 patients), there were 8 mastectomies performed, 8 NLBBs, 6 HUGs and 1 NLBB and HUG combination. One prophylactic mastectomy was performed in a patient with ADH and contralateral DCIS.

Excisional biopsy pathology

Excisional biopsy revealed that 23 (53%) of the excised lesions were malignant. Of the total of 165 specimens, 8

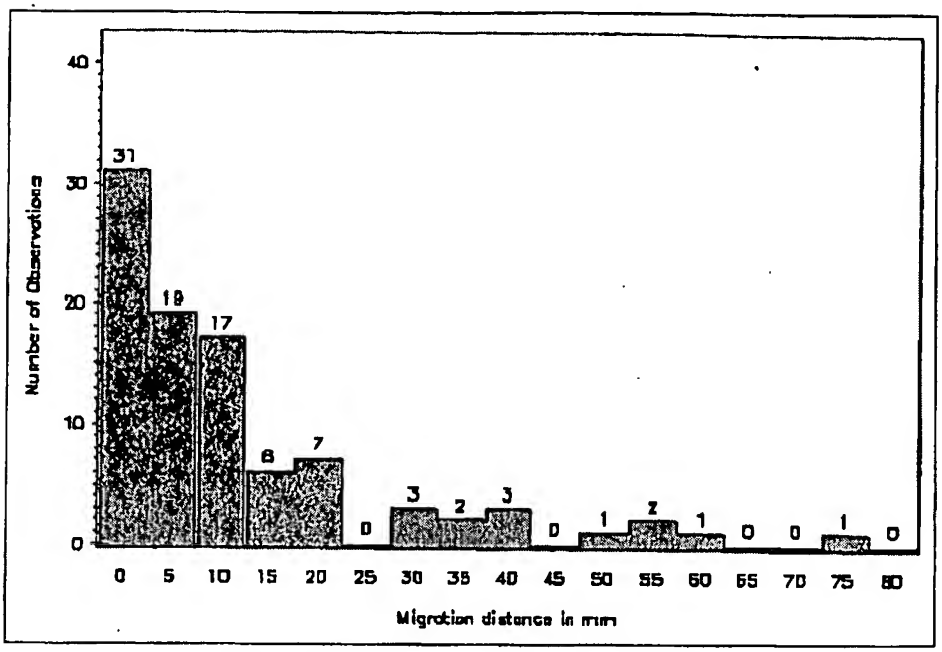

Fig. 3. Histogram of clip migration distance versus frequency.

NLBB were performed for cancer. Four specimens (50%) had negative margins, 2 (25%) had close margins, and 2 (25%) had positive margins. Six HUGs were performed for cancer. Five specimens (83%) had negative margins, none (0%) had close margins, and 1 (17%) had positive margins. One specimen performed using both NLBB and US had positive margins and was excluded from either group. In the subgroup of evaluable patients (91; 93 specimens) there were 5 NLBB that revealed malignancy. Two specimens that had negative margins had clip migration distances of only 3.5 mm and 0 mm, respectively. Two specimens with close margins had clip migration distances of 2 mm and 9 mm, respectively. One specimen with positive margins had a clip migration distance of 8.1 mm. Three specimens of the evaluable group performed by HUG revealed malignancy. All 3 specimens revealed negative margins; the clip distances for these specimens were 12.8 mm, 1 mm, and 1.6 mm, respectively.

Comments

With the current emphasis on increased screening mammography, a surgeon is frequently faced with the excision of nonpalpable breast lesions. SCNBB, first described by Parker [2] in 1990, has become the method of choice for the diagnostic biopsy of microcalcifications and other nonpalpable breast lesions. Cost savings may be as great as 50% when compared with NLBB [1,12,13]. SCNBB must be followed with a definitive procedure for cancer, atypia, other high risk lesions or when mammography and pathology are discordant [14]. Frequently, all radiographic evidence of a lesion is removed after VACB, a figure reported between 50% and 72% [8,9]. In this situation, determining the most precise method of identifying the VACB biopsy site for subsequent excision or for long term follow-up (if the core pathology proves to be benign), remains controversial. NLBB has been the traditional method for excisional biopsy after SCNBB but relies on accurate SCNBB clip placement for localization. Other alternative methods have recently been reported and will be discussed below.

This study demonstrates that significant clip migration may occur after a VACB procedure. An inaccurately located clip may contribute to positive margin status on a subsequent NLBB. HUG provides an alternative to NLBB for clips that are both correctly and incorrectly targeted.

In our study we found that clip location can be an unreliable marker for the prior VACB site. Average clip migration was calculated to be 13.4 mm with 50% of the clips placed greater that 9.5 mm and 21.5% of clips greater than 20 mm from the biopsy site. Potential for clip migration has been reported by others [9,15–18]. However, clip migration may have been underestimated due to calculation of the distance while the breast was still in compression [15,17], which would not account for the potential of clip migration once the breast is released. Measurements that involve averaging distances measured on two-view mammograms rather than deriving the actual distance as the square root of the sum of the squares also could theoretically underestimate the distance [9,18]. Our method did not factor in baseline variability that would account for slight alterations in breast positioning that occur when the breast is

placed in the "same view." This variability, determined to be 7.7 mm in one study [9], would only be applicable to our early group that employed 6 month follow-up films for measurement purposes and could have potentially led to some overestimation of distance moved in that group. Justification for using 6-month follow-up films to document clip migration (for procedures done prior to July 16, 2001) was based on a previous study that demonstrated no further clip migration after an equivalent 6-month follow-up interval [9].

There is no clear explanation for clip migration. Certainly technical problems or inexperience of the physician placing the clip can be a factor. All surgeons and radiologists performing the procedure at our institution have the recommended experience [19] with the use of the 11-gauge VACB device. Alternative explanations include accurate clip placement without attachment to surrounding tissue and either retraction with the needle or migration, versus recoil with attached tissue after release of compression. Several modifications on clip products have been devised. Microcoils have also been used to localize the site of breast lesions removed at stereotactic biopsy [20] as well as a collagen plug and clip system (MammoMark; Artemis Medical, Hayward, California) that aims to fill the biopsy cavity with collagen to limit clip movement and allow better visualization with US.

While increased use of large gauge VACB has led to improvements in the estimation of disease extent [21], it has not eliminated the need for accurate surgical excision. NLBB has been associated with positive margin status in the range of 51% to 57% [3,22]. Most positive margins after needle localization excision have been due to radiographic underestimation of disease extent [23]. However, localization on a migrated clip, rather than the true biopsy site could lead to positive margins even when specimen radiograph and pathological findings confirm both clip and biopsy site in the specimen. Although the sample size was too small to confer any significance to the findings, it was noted that two clip migrations that approached the median of 9.5 were associated with a close or positive margin status. In addition, a significant number of patients suffer problems in association with NLBB, including a miss rate ranging from 0% to as high as 22% [19,24,25], the possibility of wire transection, migration or dislocation [19,24], scheduling difficulties, vasovagal reactions in up to 20%, and the discomfort of having a wire or needle in the breast while the patient is awaiting surgery.

Alternative localization methods include carbon marking [26], use of methylene blue dye [27], radioactive seed placement [22], and the free hand needle technique [16]. The HUG technique utilizes the line of site principle and has many potential advantages over NLBB. It improves patient comfort and eliminates the need for an additional procedure with concomitant risks of complications and additional cost. Scheduling is simpler because it eliminates a visit to radiology preoperatively. The hematoma has been demonstrated to remain visible up to 56 days after biopsy, longer than the average visibility of the clip and collagen system currently available. Methylene blue dye [27] and more recently carbon marking [26] stain the biopsy site and require visual tracking and removal of the entire needle tract. Radioactive seed localization [22] requires a second procedure for location and gamma expertise but has been shown to have a lower rate of margin positivity compared with standard needle localization in a small randomized series. Radioactive seed placement is based on an accurate clip placement.

Conclusions

Achieving tumor-free margins at the first surgical excision may play a role in decreasing recurrence rate. VACB relies heavily on accurate localization of the biopsy site. In approximately 20% of cases, clip placement at the time of VACB demonstrated potentially clinically significant migration. Therefore an immediate two-view mammogram is recommended after clip placement and release of stereotactic compression to document location of clip placement in relation to the biopsy site. When performing needle localization procedures that target on the clip location physicians should first verify the accuracy of clip placement. Ultrasound-guided excision (HUG), based on VACB hematoma localization, does not require a second procedure for localization, is independent of clip position, and is a viable alternative to NLBB, especially in cases of extreme clip migration.

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Clip or Marker Migration 5–10 Weeks after Stereotactic 11-gauge Vacuum-assisted Breast Biopsy: Report of Two Cases[1]

Two women, aged 50 and 51 years, underwent stereotactic, 11-gauge vacuum-assisted biopsy from the cranial approach of small lesions in the upper outer quadrant of the right breast with removal of lesions that were detected with mammography. Postbiopsy mammograms showed the metal clip or marker at the biopsy sites in both patients. Histologic analysis of both lesions indicated atypical hyperplasia. Mammograms obtained prior to surgical excision showed caudal z-axis migration of the clip or marker to be 6.5 cm at 5 weeks and 4.5 cm at 10 weeks, respectively. By ignoring the clip or marker that had migrated to an inaccurate location and by using internal and external breast landmarks to guide presurgical excision needle localization, the biopsy sites were successfully excised in both patients.

Percutaneous stereotactic breast biopsies are increasingly being performed with an 11-gauge vacuum-assisted technique to increase histologic accuracy. This results in complete removal of many lesions, as assessed with mammography, (1–3) but does not guarantee complete removal, as assessed with histology (1,3). To aid presurgical excisional localization of malignant and high-risk lesions in need of surgical excision, a clip or marker is placed at the biopsy site when the mammographic lesion is no longer definitively seen or when the operator thinks the lesion may be difficult to find after biopsy. The initial placement of the clip or marker is usually in close proximity to the biopsy cavity but can be in a remote location (4–11). Few researchers have evaluated the relative long-term stability of clip or marker placement (4,12). Two case reports describe migration of a clip seen at initial mammographic follow-up of benign lesions 10–12 months after stereotactic 11-gauge vacuum biopsy (13,14).

Through January 2003, we have performed 4,448 stereotactic biopsies at two medical institutions with use of a prone biopsy table (Mammotest; Fischer Imaging, Denver, Colo). Biopsies of 3,531 (79%) lesions were performed with an 11-gauge vacuum-assisted biopsy device (Mammotome; Ethicon Endo-Surgery, Cincinnati, Ohio). After 11-gauge biopsy, a clip or marker was placed in 2,065 (58%) of these lesions.

We describe different types of percutaneously placed clips and markers with short-term migration noted at the time of presurgical excision needle localization for atypical hyperplasia lesions 5–10 weeks after stereotactic 11-gauge vacuum-assisted biopsy. Because of inaccurate clip or marker position and complete removal of the sampled lesion, as assessed with mammography, other mammographic landmarks were used to guide presurgical needle localization. After consultation with our Institutional Review Board, neither their approval nor informed consent were required for this study.

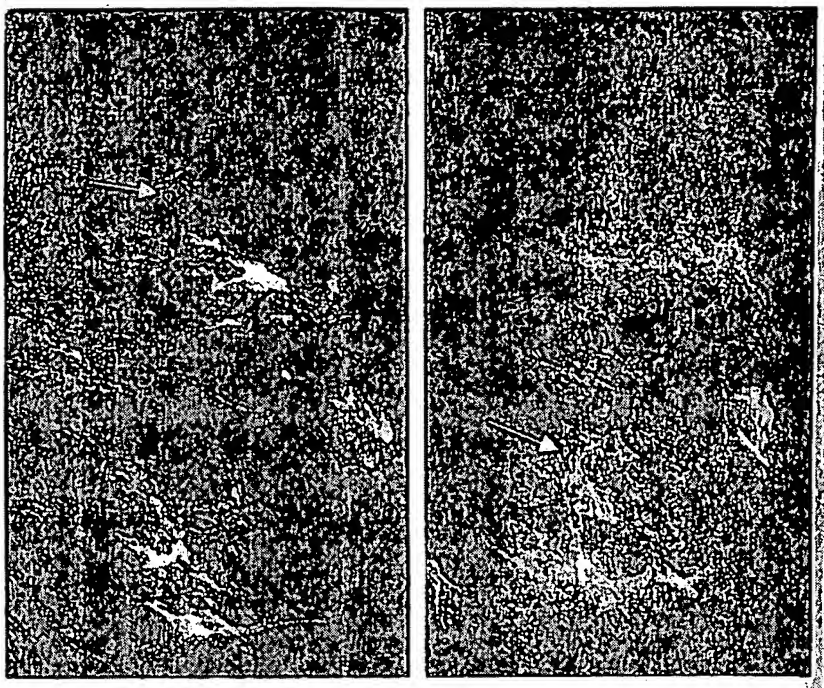
Case Report 1

A 50-year-old premenopausal woman was placed in the prone position and underwent uncomplicated stereotactic biopsy of a 10 × 12-mm indistinct mass in the upper outer quadrant of the scattered fibroglandular tissue of the right breast. Biopsy was performed with a cranial ap-

Exhibit G

proach in the craniocaudal projection by using an 11-gauge vacuum-assisted biopsy device (Mammotome; Ethicon Endo-Surgery). Sixteen samples were taken. Since the mass was no longer seen with assurance on prone stereotactic images at completion of the biopsy, a metal clip (MicroMark; Ethicon Endo-Surgery) was placed through the vacuum probe by a radiologist (R.J.J.) who has performed 887 clip or marker placements. Postprocedural stereotactic images obtained in the prone position and craniocaudal and lateral mammograms obtained in the upright position both showed the clip to be within 5 mm of the center of the biopsy site in the upper outer quadrant of the right breast and apparently adherent to tissue in the 12-o'clock portion of the biopsy cavity. Histologic analysis revealed atypical ductal hyperplasia and lobular carcinoma in situ, and surgical excision was recommended.

Five weeks after the vacuum-assisted biopsy, mammography was performed in the craniocaudal and lateral views prior to needle localization and surgical excision. The mammogram showed the percutaneously placed clip was now in the lower outer quadrant of the breast. No apparent migration was seen on the craniocaudal mammogram, but the clip had migrated 6.5 cm in the caudal direction on the lateral mammogram (Fig 1). By using all available external and internal mammographic landmarks, a localizing needle was placed at the prior vacuum site and surgical excision was performed. The clip was left in the breast. Histologic analysis of the surgically excised specimen revealed extensive involvement of ductal carcinoma in situ that extended to the margins of the excised specimen and verified removal of the vacuum-assisted biopsy site. When a larger lumpectomy-procedure performed later also revealed extensive ductal carcinoma in situ involving the specimen margins, the patient chose to undergo bilateral mastectomy.



a. b.

Figure 1. Case 1. Mammograms of a 50-year-old woman who underwent vacuum-assisted biopsy for a small indistinct mass in the upper outer quadrant of the right breast that was diagnosed as atypical ductal hyperplasia and lobular carcinoma in situ. (a) Initial postprocedure lateral mammogram demonstrates accurate clip placement (arrow). (b) Pre-needle localized surgical biopsy lateral mammogram obtained 5 weeks later demonstrates 6.5-cm caudal clip migration (arrow).

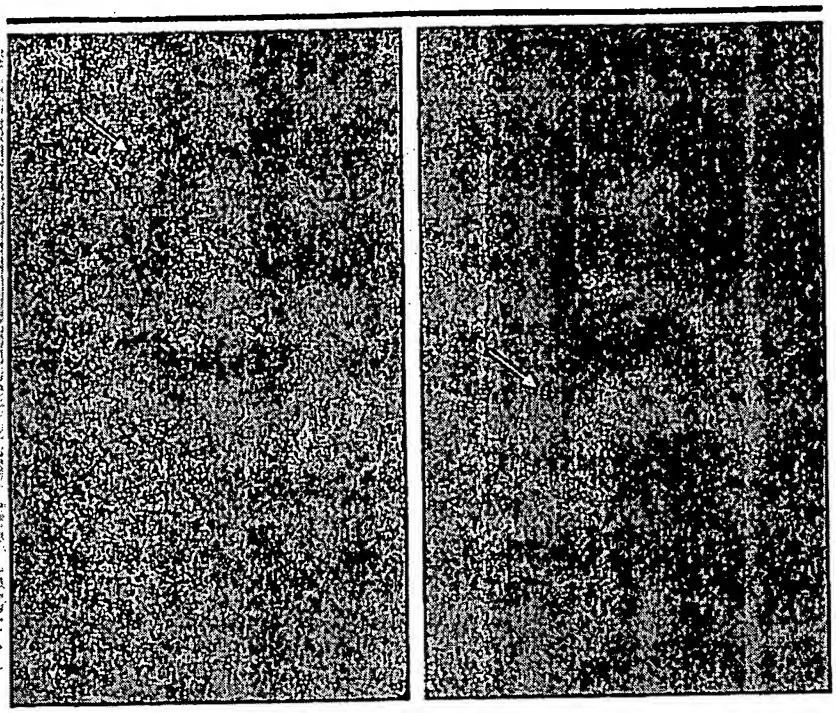
Case Report 2

A 51-year-old premenopausal woman was placed in the prone position and underwent uncomplicated stereotactic biopsy of a 3 × 4-mm cluster of pleomorphic calcifications in the upper outer quadrant of the heterogeneously dense right breast. Biopsy was performed with a cranial approach in the craniocaudal projection by using an 11-gauge vacuum-assisted biopsy device (Mammotome; Ethicon Endo-Surgery). Sixteen samples were taken, and removal of the calcifications was confirmed with a radiograph of the specimen. Since the calcifications were no longer seen on stereotactic images obtained in the prone position at the completion of biopsy, a marker consisting of seven gelatin pledgets, one of which contained a metal wire (Gel Mark; SenoRx, Aliso Viejo, Calif), was placed through the vacuum probe by a radiologist who has performed 417 clip and marker placements. Postprocedural stereotactic images obtained in the prone position and craniocaudal and lateral mammograms obtained in the upright position both showed the metal part of the marker at the center of the biopsy site, apparently within the biopsy cavity. Histologic analysis revealed atypical lobular hyperplasia, and surgical excision was recommended.

Mammography was performed in the craniocaudal and lateral planes 10 weeks after the vacuum-assisted biopsy and prior to needle localization and surgical excision. Mammography indicated the percutaneously placed marker was now in the lower outer quadrant. No apparent migration was seen on the craniocaudal image, but the marker had migrated 4.5 cm in the caudal direction on the lateral image (Fig 2). By using all available external and internal mammographic landmarks, two localizing needles were placed to bracket the site of prior vacuum-assisted biopsy, and a surgical excision was performed. The marker was left in the breast. Histologic analysis of the surgical specimen revealed atypical lobular hyperplasia without malignancy and verified that the vacuum-assisted biopsy site had been removed. Mammographic follow-up was recommended.

Discussion

Accuracy of needle-localized surgical breast biopsy is dependent on exact positioning of the localizing needle at the lesion site (15). If the mammographic lesion is completely removed with vacuum-assisted biopsy, accurate placement of a clip or marker at the biopsy site will facilitate accurate placement of the localizing needle in those lesions that require



a. b.

Figure 2. Case 2. Mammograms of a 51-year-old woman in whom atypical ductal hyperplasia was diagnosed with vacuum-assisted core biopsy. (a) Initial postprocedure lateral mammogram demonstrates accurate marker placement (arrow). (b) Ten weeks after core biopsy, pre–surgical biopsy lateral mammogram demonstrates 4.5-cm caudal marker migration (arrow).

surgical excision. In addition, accurate clip or marker placement focuses attention at mammographic follow-up on the biopsy sites of benign lesions that do not require surgical excision.

Both the MicroMark clip and the Gel Mark marker are deployed at the percutaneous biopsy site after extraction of tissue and before release of compression. Both the clip and the metal portion of the marker measure about 2 mm in diameter and are made of stainless steel that should be visible on mammograms for the life of the patient. The seven gelatin pledgets of the marker are visible on ultrasonographic (US) images for up to 20 days after the biopsy (12). Placement of the clip or marker through the indwelling probe follows vacuum suction, which clears tissue fragments and blood from both the biopsy probe and the biopsy cavity, and probe withdrawal of 5 mm. The clip is deployed during simultaneous vacuum suction that collapses the cavity, and it is designed to attach to the wall of the cavity. The marker is deployed without simultaneous use of vacuum suction, and it is designed to stay in the biopsy cavity.

Accuracy of initial clip placement after 11-gauge vacuum-assisted biopsy has been studied with stereotactic-guided biopsy (4–8) and US-guided biopsy (9). While the clip is usually in close proximity to the biopsy site, it sometimes can be in a remote location several centimeters away. Stereotactic images obtained immediately after clip placement with the breast still in compression are used to verify clip deployment (4–7) and to compare the z-axis position of the clip with the lesion (5,6). The difference in z-axis position of the lesion and the clip may cause underestimation of the inaccuracy of clip position that will be appreciated once compression is released because of the "accordion effect" (4,5,7,8). It is suggested that when the breast is released from compression, the clip can move away from the biopsy site. Movement usually occurs along the axis of needle insertion (z axis) and can be either toward or away from the skin entry site (5,6).

Accuracy of initial placement of the metal portion of the marker after 11-gauge vacuum-assisted biopsy has been studied (10,11). Initial placement was said to be more accurate with the marker (10,11) than with the clip (4,10). Good, relatively long-term stability was reported with both the clip (4) and the marker (12) in a limited number of patients.

To our knowledge, there are only two other case reports of migration of a clip, and both were noted at mammographic follow-up of benign lesions 10–12 months after stereotactic 11-gauge vacuum-assisted biopsy (13,14). We are unaware of any reports of migration of a marker.

In our two patients, clip or marker migration was apparent at the time of preneedle localization and surgical excision of atypical hyperplasia lesions 5–10 weeks after stereotactic 11-gauge vacuum-assisted biopsy. We generally advise surgical excision of both atypical ductal hyperplasia lesions (16) and atypical lobular hyperplasia lesions (17,18) that were diagnosed with percutaneous biopsy. We used a clip in one patient and a marker in the other.

If a malignant or high-risk lesion in need of surgical excision has been diagnosed at percutaneous biopsy, we focus surgical excision on the percutaneous biopsy site. If the clip or marker is in close proximity to the biopsy cavity, it can guide pre–surgical excision localization and will be removed from the specimen. If the clip or marker is in a remote position, however, as was the case in our two patients, we focus pre–surgical excision localization on the percutaneous biopsy site rather than on the clip or marker.

We obtain orthogonal mammograms in the upright position immediately prior to needle localization if placement of the clip or marker is known to be inaccurate, if mammograms obtained in the upright position immediately after the vacuum-assisted biopsy are not available, or, occasionally, to look for any residual mammographic evidence of the lesion that was sampled.

There are several factors to be considered in the course of needle localization when clip or marker position is inaccurate. If there is any residual part of the sampled lesion that is mammographically evident, we use the residual lesion to guide localization. Barring that, we perform needle localization by using all available mammographic landmarks, including the nipple, skin, calcifications, masses, vessels, and pattern of fatty and fibroglandular tissue (19). We have found that air in the breast after a percutaneous biopsy is often remote from the biopsy site, even on images obtained immedi-

ately after biopsy, and is not a reliable landmark for identification of the biopsy site. Whatever course is taken must result in accurate needle position and eventual surgical removal of the vacuum-assisted biopsy site. The fact that the percutaneous biopsy cavities were histologically found in our two surgically excised specimens suggests our localizations and subsequent surgical excisions were accurate. The histologic findings at surgery were compared with the findings at the percutaneous biopsy site and support that supposition.

In conclusion, if there is clip or marker migration and no residual mammographic lesion, we compare orthogonal mammograms obtained in the upright position before vacuum-assisted biopsy and after needle localization to ensure accuracy in the guidance of surgical excision. We try to identify the percutaneous biopsy site in the excised specimen and to correlate histologic findings in the surgical specimen with those at percutaneous biopsy to determine if the correct tissue was removed at surgery.

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Clip Migration within 8 Days of 11-gauge Vacuum-assisted Stereotactic Breast Biopsy: Case Report[1]

A 49-year-old woman underwent 11-gauge vacuum-assisted stereotactic biopsy of a cluster of indeterminate calcifications in the left breast. A clip was deployed accurately at the biopsy site as confirmed on mammograms obtained immediately after biopsy. The patient returned 8 days later for additional stereotactic biopsies of the left breast. Repeat mammograms revealed that the clip deployed at the original biopsy site had migrated 5 cm inferiorly.

Practitioners who perform stereotactic breast biopsies often choose to deploy a metallic clip near the biopsy site. This step is especially important when a malignant or high-risk lesion is entirely removed or becomes imperceptible after biopsy or when treatment involving neoadjuvant chemotherapy is planned. Misplacement of a clip is not uncommon, and it is usually noted immediately after the procedure. Two recent reports (1,2) describe clips that migrated within 10 months and 1 year of accurate placement. The purpose of this case report is to describe a clip that deviated from its original correct position at the biopsy site sometime within 8 days after the biopsy. Consultation with the institutional review board revealed that neither their approval nor informed consent was required for this case report.

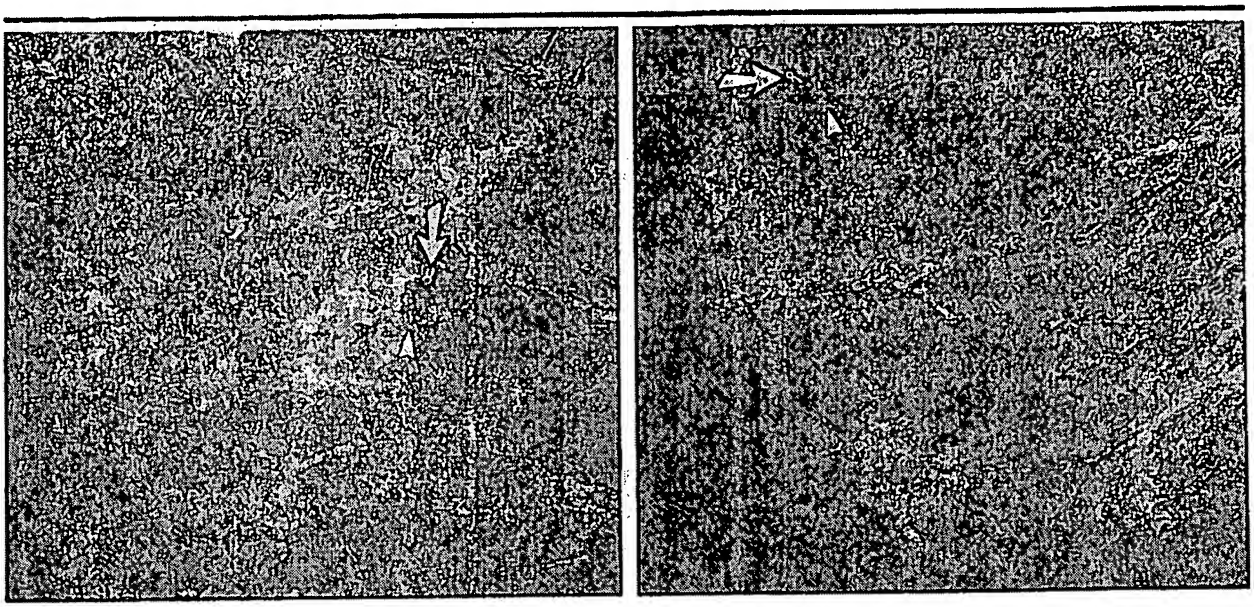
Case Report

A 49-year-old woman underwent bilateral stereotactic core biopsies, first for a spiculated calcified mass in the right breast at the 2 o'clock position, then for indeterminate calcifications in the left breast at the 2 o'clock position 5 cm posterior to the nipple. The left breast biopsy was performed from a superior-to-inferior approach in the craniocaudal projection with an 11-gauge vacuum-assisted biopsy device (Mammotome; Biopsys/Ethicon EndoSurgery, Cincinnati, Ohio). No substantial bleeding occurred during or immediately after the procedure. A metallic clip (Gel Mark; SenoRx, Aliso Viejo, Calif) was placed because all of the calcifications were removed during the biopsy. The biopsy site marker applicator contains seven dehydrated gelatin foam pledgets, the fourth of which contains a metallic clip. The gelatin foam pledgets are resorbed in approximately 1–2 weeks. The method of placement was to insert the introducer into the biopsy probe and to deploy the gelatin foam pledgets in a slow and steady manner.

Postprocedural craniocaudal (Fig 1a) and true lateral (Fig 1b) mammograms were obtained to document clip position. The craniocaudal (the projection used for the biopsy) image was obtained first to aid in the possible detection of delayed accordion-effect clip movement (1). Mammograms demonstrated removal of the calcifications, a small air-filled biopsy cavity, and the clip at the biopsy site. Pathologic analysis of the left breast revealed an early radial scar. Concurrent biopsy of the right breast revealed an infiltrating ductal cell carcinoma with calcification. When the patient was given her diagnosis 1 day later, she did not report any pain, bleeding, or swelling at the biopsy sites.

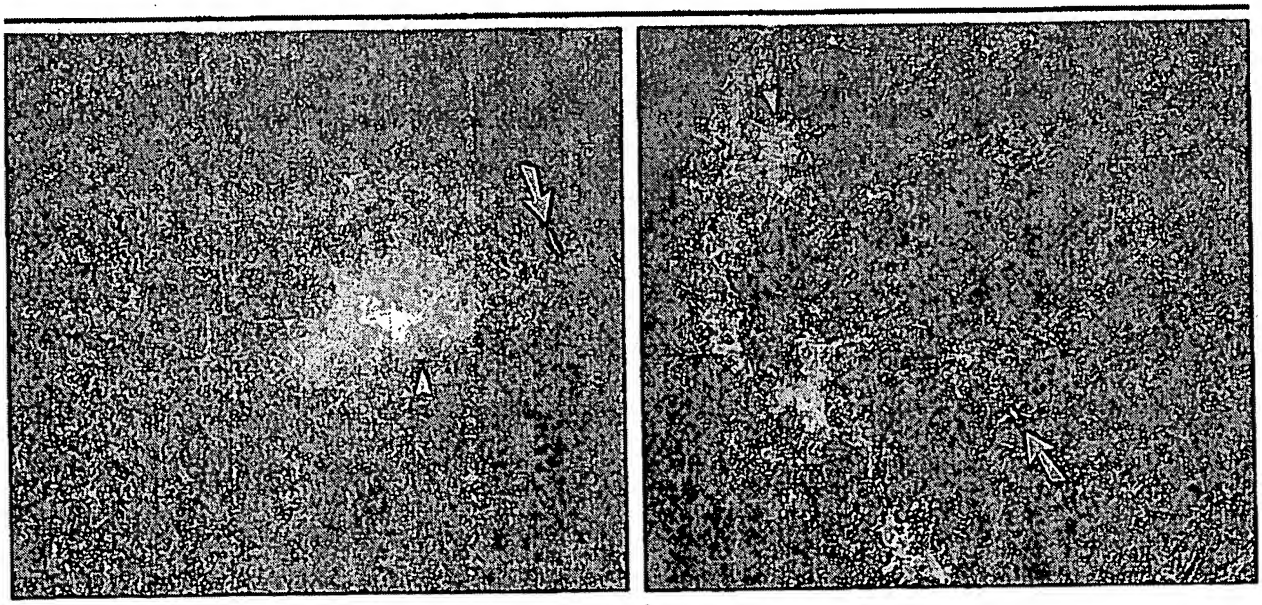
Given the contralateral malignancy of the right breast and the high-risk lesion in the left breast, the patient returned 8 days later for two additional biopsies of clusters of calcifications at separate sites in the left breast. The other procedures

Exhibit H



a. b.

Figure 1. (a) Craniocaudal and (b) true lateral postbiopsy mammograms show the clip (arrow) to be positioned correctly at the biopsy site, which is marked by an air-filled cavity (arrowhead).



a. b.

Figure 2. (a) Craniocaudal and (b) true lateral mammograms obtained 8 days after biopsy show the clip (arrow) 5 cm inferior to the biopsy site, which demonstrates a hematoma (arrowhead).

were performed from lateral to medial for calcifications at the 1 o'clock position 10 cm posterior to the nipple and at the 5 o'clock position 14 cm posterior to the nipple. The postprocedural craniocaudal (Fig 2a) and true lateral (Fig 2b) mammograms demonstrated that the clip placed accurately 8 days earlier had migrated 5 cm inferiorly and that a 1.5-cm-diameter hematoma was present.

The specimens obtained at the additional biopsies of the left breast were histologically benign. When the patient returned for needle localization, the original biopsy site in the left breast, rather than the clip, was localized.

Discussion

It is not uncommon for small lesions to become obscured or even removed af-

ter biopsy; a tissue marker is of clinical importance in cases where the histologic findings are malignant or atypical. In patients receiving neoadjuvant chemotherapy, the lesion may shrink so much that it becomes unrecognizable, and clip placement is beneficial in the event that breast conservation surgery is performed. When several lesions are present, it is of value to mark the biopsy site to allow future identification of areas already sampled at biopsy.

Unfortunately, marker clip placements are not always accurate. Marker clip misplacements, which range from millimeters to several centimeters, after stereotactic vacuum-assisted biopsies have been reported in the literature; they are usually attributed to an accordion effect along the z axis when the breast is released from compression (3–5). Although the accordion effect is usually observed immediately after the procedure, a delayed accordion effect has been described (1) in which the first postbiopsy mammogram is orthogonal to the projection in which the biopsy was performed, and the clip migrates along the needle trajectory. Bleeding during or after the procedure may also contribute to deviation of the clip. In a letter to the editor, a clip was described that had extruded through a skin incision because of bleeding (6).

In this case, the clip migrated sometime within 8 days of the biopsy, possibly as a result of a hematoma that became evident on the follow-up mammogram. Although this case is unusual in that the hematoma was not present immediately, nor was it clinically apparent 1 day later, a delayed hemorrhage is a possible explanation for the clip migration. Because the follow-up mammograms were obtained after the additional biopsies of the same breast, it could be argued that the delayed hematoma was caused by the added procedures. However, the incisions were at sites that were distant from the original location, the additional biopsies were performed in a different direction, and there was no clinical evidence of additional trauma to the original biopsy site. Therefore, it is unknown when the hematoma occurred or when the clip migrated. Other possible causes of the clip deviation include movement of the breast during everyday activities or resorption of the gelatin foam pledgets, which might allow an unanchored clip to move.

In this case, recognition of migration of the clip was crucial in the planning of the patient's subsequent needle localization procedure. Because of the large deviation from the original biopsy site, the clip was not localized. The original biopsy site was localized on the basis of landmarks within the breast that were noted on the prebiopsy mammogram. The pathology report of the excisional biopsy revealed hemorrhage.

In conclusion, clip migration, although uncommonly reported after documented accurate postbiopsy placement, is a practical concern, especially if needle localization is planned. To my knowledge, this case report is the first about clip migration that occurs after the immediate postbiopsy period, as well as the only one to involve the Ciel Mark biopsy site marker rather than the Micromark clip (Ethicon Endo-Surgery, Cincinnati, Ohio). For surgical cases in which marker clips are present, it is my opinion that repeat craniocaudal and true lateral mammograms should be obtained routinely on the day of needle localization, no matter how soon after biopsy the localization procedure is planned, because delayed clip migration could considerably change the clinical management and dramatically alter the path chosen for needle localization.

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Delayed Migration of Gel Mark Ultra Clip Within 15 Days of 11-Gauge Vacuum-Assisted Stereotactic Breast Biopsy

Jay R. Parikh[1]

Interventional breast radiologists commonly deploy metallic clips in the biopsy site after percutaneous vacuum-assisted stereotactic breast biopsy. Cases of delayed clip migration have been reported [1–6] for the MicroMark clip (Ethicon Endo-Surgery) and Gel Mark clip (SenoRx). To my knowledge, I am reporting the first case of delayed migration of the Gel Mark Ultra clip (SenoRx), which occurred within 15 days of initial accurate placement as confirmed by mammographic imaging. Sonogram-guided localization of the bioresorbable pellets enabled accurate surgical excision at the core biopsy site. Radiology–pathology correlation demonstrated that despite delayed migration of the clip, the majority of the pellets stayed near the core biopsy site, providing a reliable landmark for localization.

Consultation with the institutional review board revealed that neither their approval nor informed patient consent was required for this case report.

Case Report

A 62-year-old woman with a history of focal ductal carcinoma in situ treated in the right breast 10 years previously with lumpectomy underwent percutaneous stereotactic-guided core needle biopsy for indeterminate calcifications and associated density at 12 o'clock in the left breast. The left breast biopsy was done in a 90-degree lateral-to-medial approach with an 11-gauge vacuum-assisted biopsy device (Mammotome, Biopsys/Ethicon Endo-Surgery), as the lesion was readily identified in the lateral projection during mammographic workup, but difficult to visualize in the craniocaudal view. No significant bleeding occurred during or immediately after the biopsy. After removal of the bulk of the calcifications during core biopsy, a Gel Mark Ultra clip was deployed into the biopsy cavity.

Postprocedural mediolateral oblique images followed by craniocaudal mammographic images (Fig. 1) confirmed initial accurate clip placement at the biopsy site. Histology showed infiltrating lobular carcinoma and atypical ductal hyperplasia associated with microcalcifications in the core biopsy specimens. The patient was informed of the malignant histology by the interventional breast radiologist 2 days after biopsy and referred for surgical consultation. She reported no pain, bleeding, or swelling at the biopsy site.

The patient returned 15 days after initial stereotactic biopsy for surgical lumpectomy. Using sonographic guidance (HDI 5000 with SonoCT; Advanced Technology Laboratories), the bioresorbable pellets were localized [7] under local anesthesia with a Modified Disposable Kopans Spring Hook Localization Needle (Cook) (Fig. 2). Postprocedural true lateral and craniocaudal mammographic images (Fig. 3) confirmed successful placement of the reinforced segment of the wire in close approximation to the region of the initial biopsy cavity. However, the clip had migrated 4 cm laterally from the biopsy site. After informed consent was obtained from the patient, the clip was successfully localized with a second Modified Disposable Kopans Spring Hook Localization Needle using full-field digital mammographic guidance. Postprocedural craniocaudal and mediolateral oblique full-field digital mammographic images (not shown) confirmed successful placement of the reinforced segment of this second wire adjacent to the clip.

At surgery, the lumpectomy specimen radiograph (Fig. 4) confirmed the presence of the two hookwires and the clip. Carefully directed sectioning by the pathologist showed the malignancy and changes of the recent biopsy site to be in close approximation to the biodegradable pellets. The pathologic section containing the clip did not contain any

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Exhibit I

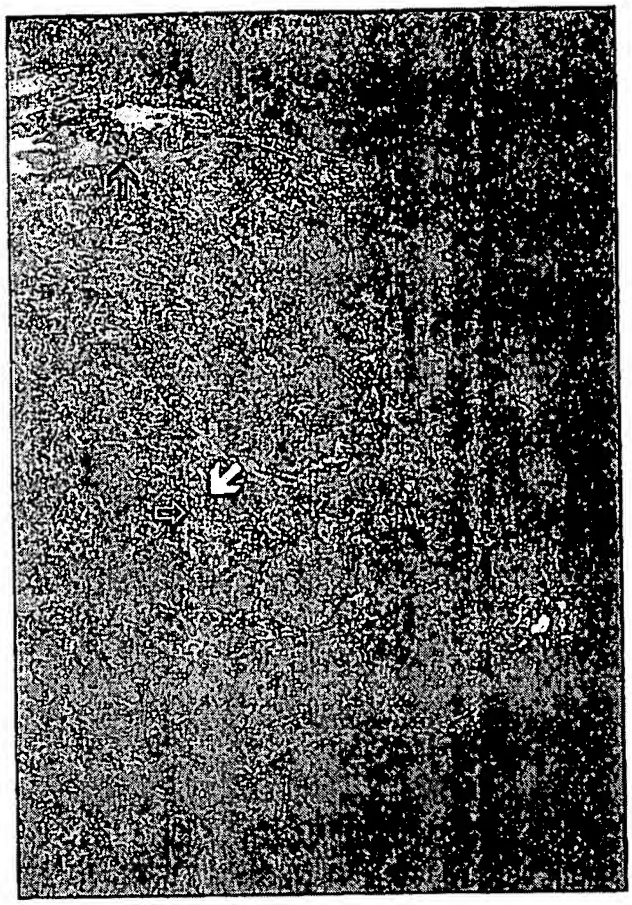

Fig. 1—Immediate postbiopsy craniocaudal film-screen mammogram in 62-year-old woman with previous history of ductal carcinoma in situ in the right breast shows Gel Mark clip (SenoRx) (*solid white arrow*) within biopsy site, as denoted by adjacent density from small hematoma (*hollow white arrow*). Air radiolucency (*solid black arrow*) is noted near stereotactic needle entry site in lateral breast.

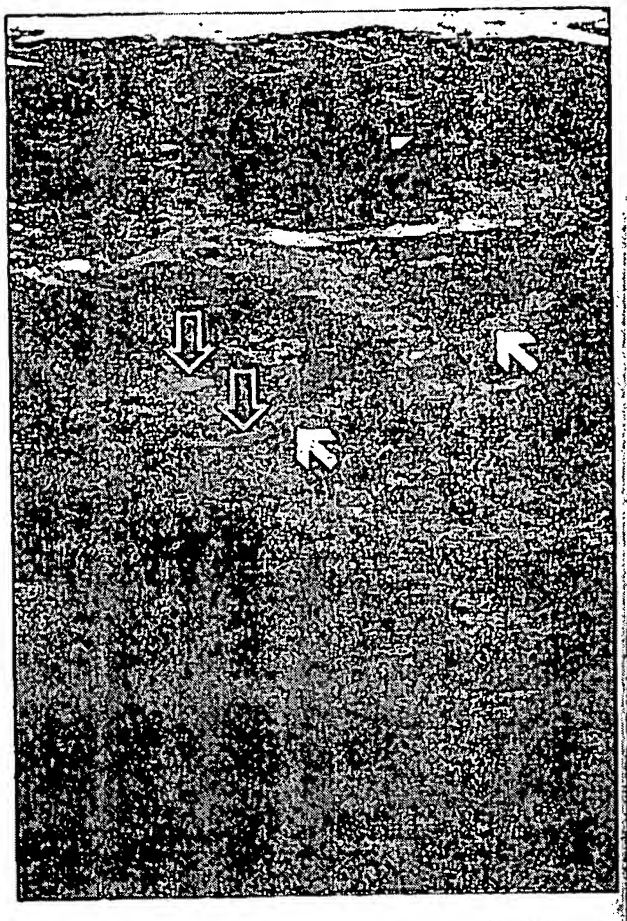

Fig. 2—With sonogram guidance, antiradial real-time compound breast sonogram image of left breast at 12 o'clock position shows needle localization wire (*solid white arrows*) placed into region of Gel Mark Ultra pellets (Seno Rx) (*hollow white arrows*) within recent stereotactic biopsy cavity.

features of the recent core biopsy. Surgical specimen histology showed residual malignancy separate from the margin. The patient's postoperative course was uneventful.

Discussion

The Gel Mark Ultra biopsy site marker system (SenoRx) consists of an introducer containing 11 biodegradable cylindric pellets. The pellets consist of a copolymer of polylactic acid and polyglycolic acid, the same basic ingredients of a Vicryl suture (Ethicon Endo-Surgery). One of the pellets contains a stainless steel clip (technical report #2, SenoRx). Immediately after a stereotactic breast biopsy, the introducer system is placed into the biopsy probe, and the pellets are deployed into the biopsy cavity in a slow and steady manner. Embedded within the pellets are carbon dioxide bubbles that make the marker highly echogenic and visible on sonography for at least 4 weeks [8]. This enables sonographically-guided needle localization when necessary after stereotactic breast biopsy [7]. The pellets are ultimately degraded and resorbed, with the permanent metallic clip left behind.

Delayed migration is an increasingly recognized complication of clip placement, and refers to the shift of the marker location after initial correct placement of the marker into the biopsy cavity. At least four cases of delayed migration of the MicroMark clip within 5 weeks [1], 6 weeks [2], 10 months [3] and 1 year [4] of accurate initial placement have been reported. Similarly, delayed migration of the Gel Mark clip within 8 days [5], 15 days [6], and 10 weeks [1] of initial accurate placement has been reported.

To my knowledge, this is the first report of delayed migration of the Gel Mark Ultra clip, which occurred within 15 days of initial accurate placement confirmed by mammographic imaging.

The delayed migration of the Gel Mark Ultra clip in this case was along the axis of the insertion of the biopsy needle (i.e., the Z axis). This has been postulated to occur from the accordion effect [9]. In theory, immediately after the core biopsy, the clip is within the biopsy cavity but does not adhere firmly to the breast tissue. When the breast is released from compression after stereotactic biopsy, the metallic-clip shift from the biopsy site occurs along the trajectory of the biopsy

Fig. 3—Initial preoperative needle localization craniocaudal mammogram shows localization wire to be in region of biopsy cavity; minimal hematoma is present (*hollow arrow*). Skin entry site of hookwire is denoted by round metallic BB placed on patient. Gel Mark clip (SenoRx) (*solid white arrow*) has laterally migrated with respect to biopsy site. Ill-defined density (*solid black arrow*) is present in mammogram from infiltrated local anesthesia.

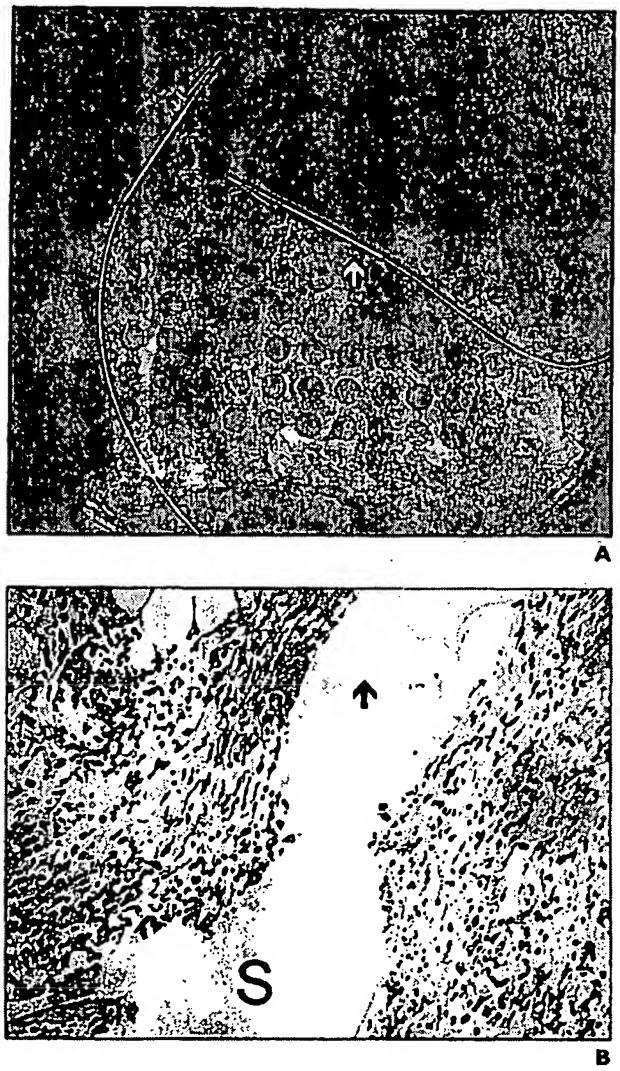

Fig. 4—Mammogram specimen.
A, Photomicrograph of localized clip (*solid white arrow*) and both hookwires in surgical excision. (H and E, ×100)
B, Translucent material from pellets (*solid black arrow*) within elongated space (*black S*) is seen, representative of core needle biopsy cavity surrounded by fibrosis and inflammation. In region of core biopsy site, pattern consistent with infiltrating lobular carcinoma (not shown) was identified. After carefully supervised sectioning by interpreting pathologist, no malignancy was found in region of migrated clip.

needle, presumably the axis of least resistance. Other possible mechanisms of clip migration include simple migration of the clip in fatty tissue, bleeding during or after the procedure displacing the clip, and resorption of postbiopsy air [9].

In this case, preoperative sonographically-guided needle localization of the pellets [7] enabled successful surgical excision of the core biopsy site and malignancy, despite clip migration. Initial postprocedure mammographic images confirmed the localization hookwire to be adjacent to the biopsy cavity, whereas the clip had migrated 4 cm from the core biopsy site. Radiologic–pathologic correlation demonstrated that the majority of pellets had stayed within the biopsy cavity, whereas the metallic clip had migrated. Based on this experience, radiologists should consider sonographically-guided localization of the Gel Mark Ultra clip a viable option compared with mammographic guidance. This approach may be especially helpful in the settings of clip mi-

gration and/or mammographic disappearance of the initial lesion after stereotactic core needle biopsy. Further research is needed to assure that the sonographically visible pellets do not migrate.

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Case Report

Clip Migration Within 15 Days of 11-Gauge Vacuum-Assisted Stereotactic Breast Biopsy

Jay Parikh[1]

After a percutaneous vacuum-assisted breast biopsy, a metallic clip is frequently placed at the biopsy site by interventional breast radiologists [1, 2]. The clip acts as a landmark for future reference when the mammographic abnormality (mass or calcifications) is removed during stereotactic biopsy. If histology is benign, the clip denotes the site of biopsy on future mammograms. If atypical or malignant histology is found at the core biopsy, the clip helps to identify and localize the area as needed for future surgery. With neoadjuvant therapy, a malignant area can become progressively and mammographically imperceptible, with the clip remaining as the only mammographic evidence of the initial site of the malignancy.

Initial clip misplacement at the time of stereotactic breast biopsy is known to occur [3] and is typically identified immediately after the procedure. Three reports of migration of the MicroMark clip (Ethicon Endo-Surgery) within 5 weeks [4], 10 months [5], and 1 year [6] of accurate initial placement have been reported. Two cases of migration of the Gel Mark clip (SenoRx) within 8 days [7] and 10 weeks [4] of initial accurate placement have been reported [6]. To my knowledge, I am reporting the first case of Gel Mark clip migration, which occured within 15 days of initial accurate placement that was confirmed by mammographic imaging, that led to inaccurate preoperative needle localization, using digital stereotactic guidance.

Consultation with the institutional review board revealed neither their approval nor informed patient consent was required for this case report.

Case Report

A 60-year-old woman with no family or personal history of breast cancer and a previous benign stereotactic breast biopsy in the right breast underwent percutaneous stereotactic-guided biopsy for indeterminate calcifications at the 11-o'clock position of the right breast. The right breast biopsy was done in a cranial to caudal approach with an 11-gauge vacuum-assisted biopsy device (Mammotome, Biopsys/Ethicon Endo-Surgery). No significant bleeding occurred during or immediately after the biopsy. A metallic Gel Mark clip was deployed into the biopsy cavity because of removal of the bulk of the calcifications during biopsy. This biopsy site marker system consists of an introducer containing seven dehydrated gelatin foam pledgets, the fourth of which contains a stainless steel clip. The introducer system is placed into the biopsy probe and the foam pledgets are deployed into the biopsy cavity in a slow and steady manner. The gelatin foam pledgets are ultimately resorbed, with the clip left behind.

Postprocedural craniocaudal images followed by mediolateral oblique mammographic images (Fig. 1) confirmed removal of calcifications on biopsy with accurate initial clip placement at the biopsy site. An air-filled cavity and minimal hematoma changes were present after biopsy. Histology showed atypical ductal hyperplasia associated with microcalcifications in the core biopsy specimens. The patient was contacted 1 day after biopsy and reported no pain, bleeding, or swelling at the biopsy site. She was informed of the histologic results and surgical excision after preoperative needle localization was recommended.

The patient returned 15 days after initial stereotactic biopsy for surgical excisional biopsy. Preoperative needle localization was done with digital stereotactic guidance with a modified disposable Kopans spring hook localization needle (Cook), using the same craniocaudal approach. The skin-entry site of the localizing needle was close to the scar from recent stereotactic breast biopsy. Postprocedural craniocaudal and true lateral mammographic images (Fig. 2) confirmed successful placement of the reinforced segment of the wire in close approximation to the clip. However, the clip had migrated 8 cm inferiorly, 1 cm laterally, and 1 cm posteriorly with respect to the initial biopsy site. The mammographic images, clip migration, and

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Exhibit J

wire placement were all immediately discussed with the patient and breast surgeon.

After informed consent was obtained, the biopsy site was successfully localized stereotactically using a craniocaudal approach with a second modified disposable Kopans spring hook localization needle. Postprocedural craniocaudal and true lateral mammographic images (Fig. 3) confirmed successful placement of the reinforced segment of this second wire in close approximation to the hematoma at the biopsy site.

At surgery, the errant wire localizing the migrated clip was removed by the surgeon. A specimen containing the correctly placed

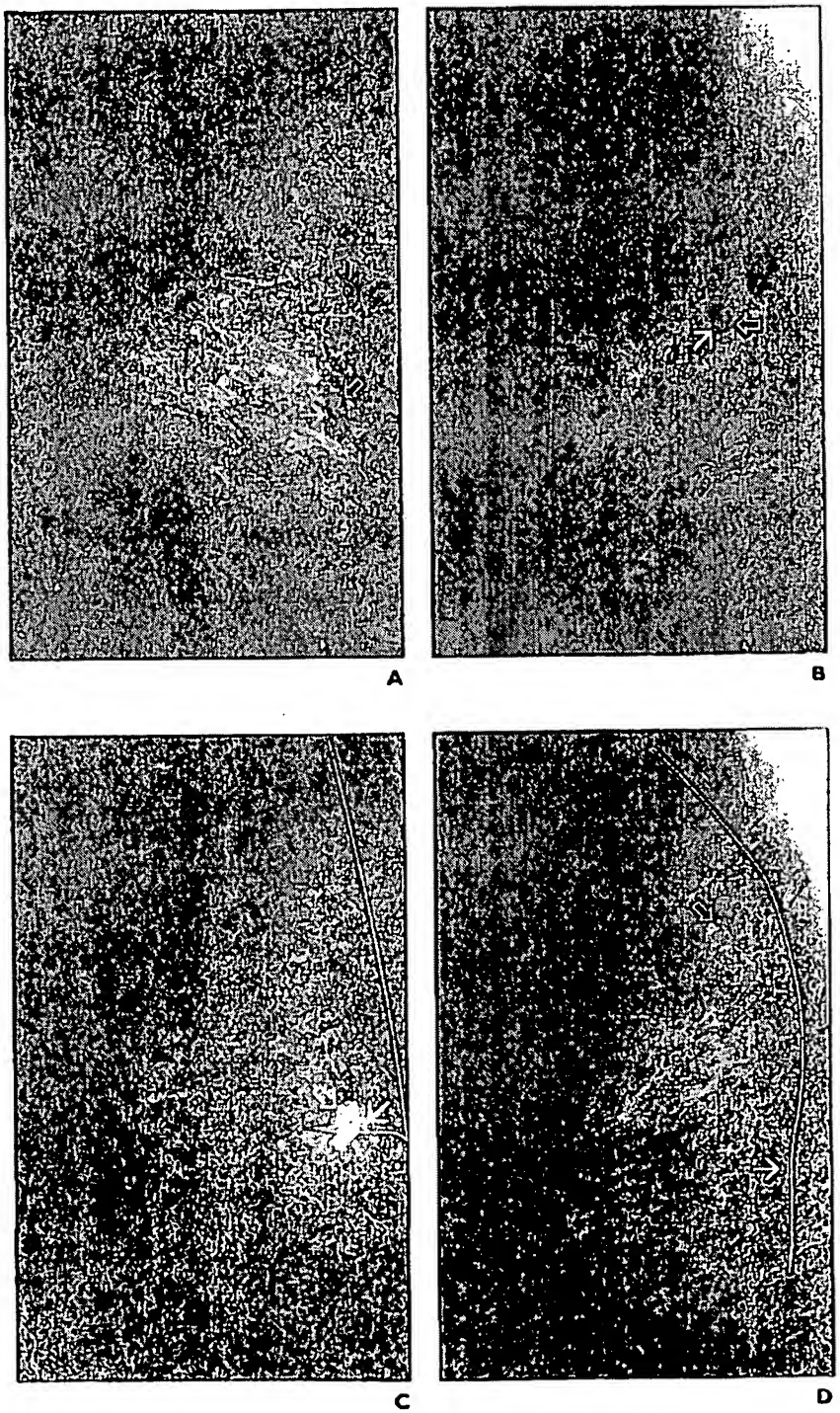
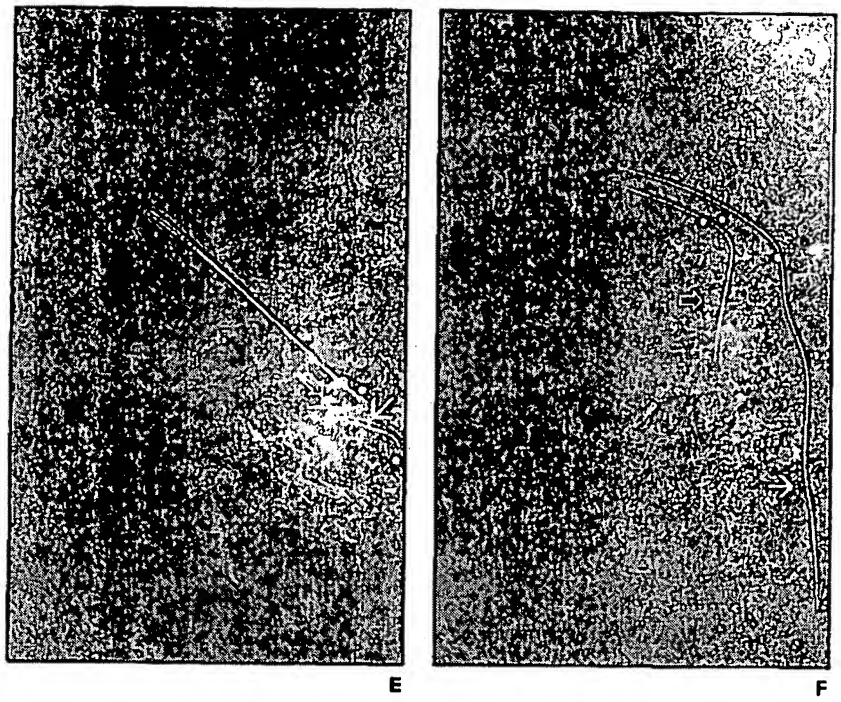


Fig. 1.—A 60-year-old woman with no family or personal history of breast cancer and a previous benign stereotactic breast biopsy in the right breast underwent percutaneous stereotactic-guided biopsy for indeterminate calcifications at the 11 o'clock position of the right breast.
A and B, Immediate postbiopsy craniocaudal (A) and true lateral (B) mammograms show the Gel Mark clip (SenoRx) (*white arrow*) to be within biopsy site, as denoted by air-filled cavity (*hollow white arrow*). MicroMark clip (Ethicon Endo-Surgery) from remote stereotactic biopsy (*black arrow*) is noted.
C and D, Initial preoperative needle localization craniocaudal (C) and 90-degree lateral (D) mammograms show Gel Mark clip (Seno Rx) (*arrow*) to be inferiorly, laterally, and posteriorly displaced with respect to biopsy site, where there is minimal hematoma (*hollow arrow*). Initial hookwire placed under stereotactic guidance is shown in close approximation to clip, with skin-entry site denoted by round metallic BB placed on breast.
(Fig. 1 continues on next page)



E F

Fig. 1. (continued)—A 60-year-old woman with no family or personal history of breast cancer and a previous benign stereotactic breast biopsy in the right breast underwent percutaneous stereotactic-guided biopsy for indeterminate calcifications at the 11 o'clock position of the right breast.
E and F, Final preoperative needle localization craniocaudal (E) and mediolateral oblique (F) mammograms again confirm Gel Mark clip (Seno Rx) (*arrow*) to be inferiorly, laterally, and posteriorly displaced with respect to biopsy site, where there is minimal hematoma (*hollow arrow*). Second hookwire placed under stereotactic guidance is through biopsy site, with skin-entry site denoted by two round metallic BBs placed on breast.

wire containing the biopsy site was surgically excised. Histologically, the surgical biopsy specimen showed fibrosis, fat necrosis, hemorrhage, and chronic inflammation consistent with the previous biopsy site. No residual foci of atypical ductal hyperplasia were seen in the specimen, and microcalcifications were associated with benign adenosis. No intraductal or infiltrating malignancy was identified. The postoperative course was uneventful.

Discussion

Tissue marker clip placement after percutaneous stereotactic breast biopsy is often used by interventional breast radiologists [1, 2]. If a lesion becomes mammographically obscured or absent immediately after percutaneous stereotactic breast biopsy, a clip is commonly introduced through the biopsy needle into the biopsy cavity to help enable future localization if core biopsy histology shows malignancy or high-risk lesions. A clip may represent the only mammographic evidence of the initial biopsy site after neoadjuvant therapy. Clip malposition is becoming increasingly recognized as a complication after percutaneous stereotactic breast biopsy. This may be from initial misplacement of the clip at the time of the biopsy or from delayed migration.

Initial clip misplacement at the time of stereotactic breast biopsy is usually identified immediately after the procedure. This initial clip misplacement typically ranges from a few millimeters to centimeters for the MicroMark clip and is largely attributed to the accordion effect along the z-axis during decompression of the breast after stereotactic biopsy [3]. Thus, initial clip misplacement is along the same axis as the needle trajectory. One letter [8] describes clip extrusion through the skin-entry site after stereotactic breast biopsy.

Delayed migration refers to shift of the marker location after initial correct placement of the marker into the biopsy cavity. Three reports of delayed migration of the MicroMark clip within 5 weeks [4], 10 months [5], and 1 year [6] of accurate initial placement have been reported. Two cases of migration of the Gel Mark clip within 8 days [7] and 10 weeks [4] of initial accurate placement have been recently reported. This article reports a third such migration of this clip that occurred within 15 days of initial accurate placement confirmed by mammographic imaging. To my knowledge, this is the first such migration that led to inaccurate preoperative needle localization.

The two previous reports of delayed migration of the Gel Mark clip have been along the axis of the insertion of the biopsy needle (i.e., the z-axis). This has been postulated to occur from the accordion effect. Initially at biopsy, the clip is within the biopsy cavity but does not adhere firmly to the breast tissue. When the breast is released from compression after stereotactic biopsy, movement of the clip from the biopsy site occurs along the trajectory of the biopsy needle, presumably the axis of least resistance.

The mechanism of delayed migration of the Gel Mark clip in the presented case is more complex. The migration of the Gel Mark clip in this patient was shown by mammography to be 8 cm inferiorly, 1 cm laterally, and 1 cm posteriorly. This movement in three dimensions (x, y, z) cannot be solely replaced by the accordion effect, which occurs along the z-axis. Some of this shift may be due to pliability of the breast and technical factors, such as slightly different angles of compression of the same projection during different mammograms. Minimal hematoma changes were noted at the stereotactic biopsy site on the immediate postbiopsy and preoperative mammogram images. Bleeding during or after the procedure may have contributed to shift of the clip. In addition, asymmetric resorption of the gelatin foam pledgets may have contributed to clip deviation.

In this case, delayed clip migration within 15 days of initial placement of the Gel Mark clip led to inaccurate initial preoperative stereotactic-guided needle localization. Based on this experience, as Philpotts et al. [6] recommend, I strongly recommend that repeat craniocaudal and lateral mammograms be obtained on the day of the needle localization before the procedure. This should be done irrespective of how soon after the biopsy the needle localization is scheduled. Unanticipated delayed clip migration can otherwise lead to inaccurate preoperative needle localization, dramatically affecting patient care.

Other methods can also be used to help assure accurate preoperative needle localization, even if there is delayed migration. If one is using digital stereotactic guidance with the same approach and equipment as the original stereotactic biopsy, the z-axis depth of the clip on the day of the localization can be compared with the z-axis depth of the lesion on the date of biopsy to determine significant z-axis migration. If mammographic-guided localization is done, the orthogonal view to the initial approach of biopsy enables comparison of the depths of the localizing needle, the clip, and the location of the lesion on the prebiopsy views. If sonogram guidance is used, the postbiopsy hematoma can be localized.

To summarize, a 60-year-old woman underwent 11-gauge vacuum-assisted stereotactic biopsy of a cluster of indeterminate calcifications in the right breast. Initial clip placement was confirmed by mammography to be at the biopsy site. The clip was localized for surgery stereotactically 15 days later, which confirmed interval migration of the clip in three dimensions. The delayed clip migration led to inaccurate preoperative needle localization. Based on this experience, radiologists are recommended to obtain orthogonal mammogram on the day of needle localization before wire placement, irrespective of the time interval after initial stereotactic-guided clip placement.

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Fred Burbank, MD • Nancy Forcier, MD

Tissue Marking Clip for Stereotactic Breast Biopsy: Initial Placement Accuracy, Long-term Stability, and Usefulness as a Guide for Wire Localization[1]

PURPOSE: To determine initial placement accuracy, long-term stability, and usefulness as a guide for wire localization for metallic marker clips placed percutaneously after stereotactic breast biopsy.

MATERIALS AND METHODS: One hundred forty-nine marker clips were placed percutaneously with a straight-needle or through-probe method, and clip positions were measured. The locations of 31 marker clips were followed up from deployment to first follow-up mammography. Thirty-six biopsy sites with marker clips were excised surgically and examined; 18 of these marker clips were targets for wire localization. The locations of 22 benign lesions were measured over time to calibrate the measurement system.

RESULTS: Baseline variability was 8 mm. Initial marker clip deployment averaged 5 mm above baseline from the center of the target lesion ($P \leq .01$). Compared with baseline variability, marker clips remained in place from initial deployment to first imaging follow-up (mean, 8.6 months). Potentially clinically meaningful misplacement rates (deployment > 24 mm from target lesion center) were 7% for the through-probe method and 11% for the straight-needle method (not significantly different; $P = .33$).

CONCLUSION: The marker clips appear to be useful targets for wire localization when the entire target lesion is removed at directional, vacuum-assisted breast biopsy. Upright, two-view mammography is recommended after deployment of the marker clip to document location.

WHEN percutaneous breast biopsy was first performed with fine-needle aspiration to establish a cytologic diagnosis for a mammographically identified lesion, the concern that fine-needle aspiration would remove the entire target lesion was not addressed, to our knowledge. Conversely, insufficient acquisition of tissue has become the "Achilles' heel" of fine-needle aspiration breast biopsy (1). After the introduction of automated core needle breast biopsy by Parker et al (2) in 1990, concern that a small target lesion might be removed entirely with use of this technique led Dershaw (3) and Sullivan (4) to recommend that automated core needle breast biopsies be performed only on lesions greater than 5 mm in diameter.

Dronkers (5) reported that in six (8.6%) of 70 18-gauge automated core needle breast biopsies (Crown-Core-Cut Needle; Biomed Instrumente Produkte, Turkenfeld, Germany), "... the lesion disappeared after the stereotactic biopsy". Similarly, Mikhail and colleagues (6) reported that in 60 lesions in which breast biopsy was performed with a 14-gauge automated core needle (Biopty-Cut Needle; Bard Gynecology and Radiology, Covington, Ga), three (5%) lesions were malignant and "... were so small that the ... needle biopsy completely removed the focus of malignant cells ...".

An even higher frequency of total excision of all visible target lesion landmarks has been reported after directional, vacuum-assisted breast biopsy. In a study in which 14-gauge directional, vacuum-assisted probes (Mammotome; Biopsys Medical, Irvine, Calif) were used (these probes remove 35–45 mg of tissue per specimen), Burbank reported that 50% of the target lesions could not be identified mammographically immediately after stereotactic breast biopsy and that 48% of the lesions could not be identified at the first imaging follow-up months after the stereotactic biopsy (7,8). Excisional breast biopsies that demonstrate histologically clear margins of atypical ductal hyperplasia, ductal carcinoma in situ, and infiltrating breast cancer for lesions 5 mm in diameter and smaller have been reported in 30% of the 14-gauge directional, vacuum-assisted breast biopsies (9).

Furthermore, directional, vacuum-assisted breast biopsies are now being performed percutaneously with 11-gauge probes. The 11-gauge probe removes approximately 90–100 mg of tissue per specimen (10). At this level of percutaneous removal of breast tissue, all visible signs of the target lesion may be removed at an even higher frequency than reported previously.

When total removal of the target lesion occurs during a diagnostic percutaneous stereotactic breast biopsy and the target lesion proves to be

Index terms: Biopsies, technology, 00.1261, 00.1267 • Breast, biopsy, 00.1261, 00.1267 • Breast neoplasms, diagnosis, 00.31, 00.32 • Stereotaxis, 00.1267

Radiology 1997; 205:407–415

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F.B. and N.F. are shareholders in Biopsys Medical.

See also the article by Liberman et al (pp 417–422) in this issue.

Exhibit K

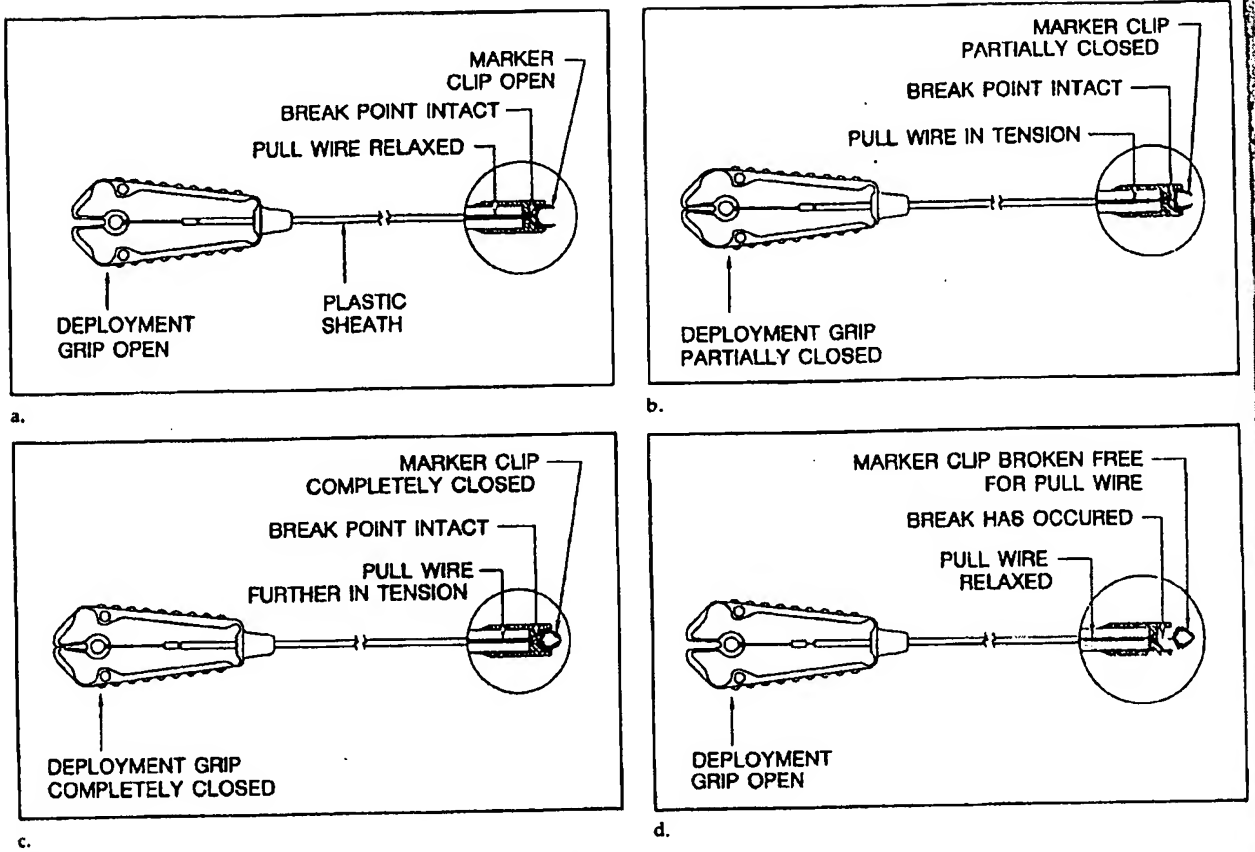


Figure 1. Diagram shows the closure sequence of the marker clip.

atypical ductal hyperplasia, ductal carcinoma in situ, or infiltrating breast cancer, the question remains as to how the biopsy site can be identified accurately for presurgical wire localization. Another question remains as to how the biopsy site can be identified unambiguously during 3 or more years of imaging follow-up when the target lesion proves to be benign.

To address the problem of total removal of a target lesion during directional, vacuum-assisted stereotactic breast biopsy, a 15-gauge, 2 × 2-mm, percutaneous metallic marker clip was developed (MicroMark; Biopsys Medical) and approved by the US Food and Drug Administration on March 15, 1995 for placement in soft tissues. The marker clip and deployment system adds a cost of $75 and approximately 1–2 minutes to the stereotactic breast biopsy procedure.

The purpose of this study was to determine (*a*) the initial accuracy of placement of a marker clip immediately after directional, vacuum-assisted breast biopsies; (*b*) stability of the marker clip after placement from time of insertion to the first follow-up mammographic study; and (*c*) the usefulness of the marker clip as a mammographic guide during wire localization before therapeutic breast surgery.

MATERIALS AND METHODS

A total of 171 patients were studied; 22 patients (average age, 46.8 years; range, 38–85 years) contributed benign control lesions for calibration of the measurement system. In 149 patients (average age, 53.5 years; range, 32–86 years), biopsy was performed with a 14- or 11-gauge directional, vacuum-assisted probe (Biopsys Medical) and marker clips were placed. Between December 8, 1995, and January 28, 1997, 49 (33%) directional, vacuum-assisted biopsies were performed with 14-gauge directional, vacuum-assisted probes and 100 (67%) biopsies were performed with 11-gauge probes. Two radiologists (F.B., N.F.) performed all marker clip placements. The details of performing a directional, vacuum-assisted breast biopsy have been published previously, including complication rates (10,11). Each patient gave informed consent before undergoing biopsy and receiving a marker clip.

Aggregate specimen weights were measured and reported by the attending pathologist at Mission Hospital Regional Medical Center as part of the gross pathologic description for each directional, vacuum-assisted breast biopsy sample. Directional, vacuum-assisted biopsies were categorized as excisional or incisional by examining two ×8 magnified stereotactic digital mammograms and two upright, craniocaudal and mediolateral oblique mammograms obtained after biopsy and marker clip placement. If no residual signs of the target lesion were seen on either of these two sets of mammograms, the biopsy was categorized as excisional. If residual signs of the target lesion were present, the biopsy was categorized as incisional.

Figure 1 shows the percutaneous 2 × 2-mm marker clip and marker clip assembly. The marker clip has two shapes, depending on whether it is open or closed. When open, the marker clip resembles a tiny horseshoe. When closed, the two limbs of the horseshoe are pinched together, forming a diamond shape. The marker clip assembly consists of a deployment grip, a pull wire attached to the deployment grip at one end and attached to the marker clip at the other end, and a plastic sheath that separates the deployment grip from the marker clip. As tension is applied to the pull wire by squeezing the deployment grip, the marker clip changes from the open shape to the closed shape. When breast tissue is trapped between the limbs of the marker clip, the

marker clip is then attached or "clipped" to that tissue similar to the action of a surgical vascular clip. As progressively more tension is applied, the marker clip breaks free from the pull wire. At deployment, the marker clip is free from the deployment assembly and is attached to breast tissue at or near the directional, vacuum-assisted breast biopsy site. For purposes of description, the marker clip deployment sequence is shown as four separate steps. In practice, the process occurs almost instantaneously (one rapid motion).

Two marker clip deployment methods were used in this study. The first marker clip deployment method is referred to as the "straight-needle" method. The second deployment method is referred to as the "through-probe" method.

For the straight-needle deployment method, six steps were necessary: (*a*) a directional, vacuum-assisted biopsy was performed with a 14-gauge probe (43 deployments) (11); (*b*) the directional, vacuum-assisted probe and motorized probe driver were removed from the stereotactic breast biopsy table and set aside; (*c*) a purpose-built needle holder was placed on the stereotactic breast biopsy table (this needle holder was secured to a straight 13-gauge needle with a pointed, bevel-tipped trocar); (*d*) a new set of coordinates was generated by the computer to position the tip of the straight needle at the biopsy site; (*e*) the straight needle with a central trocar was advanced to the biopsy site; and (*f*) the trocar was removed and the percutaneous marker clip assembly was advanced down the shaft of the straight needle, and the marker clip was attached to the wall of the biopsy cavity as shown in Figure 1.

The through-probe deployment method consisted of two steps: (*a*) directional, vacuum-assisted biopsy was performed with a 14-gauge probe (six deployments) or an 11-gauge probe (100 deployments); and (*b*) the marker clip assembly was advanced through the directional, vacuum-assisted probe, and the marker clip was attached to the wall of the biopsy cavity as shown in Figure 1.

To evaluate accuracy of marker clip placement and placement stability over time, a measurement system was needed to describe accurately the location of the marker clip and the target lesion within the breast. The American College of Radiology Breast Imaging and Reporting System contains a breast lesion location system (12). Although this method is suitable for generally defining the location of a lesion within the breast, it is not suitable for describing small differences in the position of two objects that may be close to one another within the breast. Consequently, we developed and tested a new measurement system, the "mask measurement system."

The mask measurement system transfers information from two mammograms to one sheet of clear x-ray film referred to as the "mask." After information is hand-traced from the two mammograms to the mask, the mask contains information from both mammograms. The first mammogram defines the shape of the breast and the location of an object of interest on the mask. The second mammogram is fitted to the mask, and the object of interest on the second mammogram is drawn on the mask. The objects of interest, whose locations are compared on the masks, can be a target lesion and a marker clip (first context, described later), a marker clip at two points in time (second context), or a target lesion at two points in time (third context).

If the position of an object within the breast was identical on two mammograms and if the breast projected to the same location on each mammogram, then two tracings of the objects on the mask would superimpose exactly. In this idealized example, the tracings of the superimposed objects on the mask could be described as exactly "on target." However, a breast never projects as exactly the same shape on any two mammograms. Furthermore, when a marker clip is placed in the breast, it may or may not embed in the desired location. Finally, even if the marker clip is deployed accurately, it may move from one location to another over time. When the tracing of an object is not in the ideal position on the mask, the object is described as "off target." The distance (in millimeters) that an object is off target is measured directly on a mask with a ruler.

The craniocaudal mask describes the distance off target in one projection; the mediolateral oblique mask describes the distance off target in another projection. To combine the information from the craniocaudal and mediolateral oblique mammogram masks, a single, continuous, dependent variable was defined and referred to as the "average distance off target." The average distance off target has three meanings, depending on three contexts.

Initial Accuracy of Marker Clip Deployment

In the first context, the average distance off target of the marker clip with respect to the target lesion immediately after stereotactic directional, vacuum-assisted breast biopsy and deployment of the marker clip was measured by creating a mask of the craniocaudal and mediolateral oblique mammograms obtained before biopsy. The mask for each projection was created by stapling a clear sheet of x-ray film on top of the craniocaudal and mediolateral oblique mammograms obtained before biopsy (Fig 2a). With use of a bright light, the skin line, the nipple, and an outline of the lesion were traced by hand onto the mask with an indelible film marker (Fig 2b). For mass lesions, the lesion borders were traced; for clustered microcalcification lesions, the outermost edges of the cluster were traced. The center of each lesion was marked with a dot.

After directional, vacuum-assisted biopsy was performed, the marker clip was delivered percutaneously at or near the biopsy site by means of the straight-needle (43 deployments) or through-probe (106 deployments) deployment method. Craniocaudal and mediolateral oblique mammograms were obtained immediately after biopsy and marker clip deployment to define the locations of the marker clip within the breast in the craniocaudal and mediolateral oblique projections (Fig 2c). The target lesion was commonly removed entirely, distorted, or obscured as a result of the directional vacuum-assisted biopsy. Consequently, the target lesion was often no longer visible or identifiable on the mammograms obtained after biopsy and marker clip placement. The marker clip, however, was always clearly visible.

Finally, the craniocaudal mask was placed on top of the craniocaudal mammogram obtained after biopsy and marker clip placement, and the mediolateral oblique mask was placed on top of the mediolateral oblique mammogram obtained after biopsy and marker clip placement. The skin outlines from each corresponding mask and mammogram obtained after biopsy were fitted together with use of a bright light and the position of the nipple as the fulcrum to achieve the best overall "fit." Once the fit was optimal, the position of the marker clip was drawn as a diamond on the craniocaudal and mediolateral oblique masks with an indelible marker (Fig 2d).

The craniocaudal and mediolateral oblique masks then contained the locations of the two objects of interest: the target lesion and the marker clip. The distance from the center of the target lesion to the center of the marker clip was measured (in millimeters) on the masks in the craniocaudal and mediolateral oblique projections (Fig 2d). The distances between the target lesion and the marker clip in the craniocaudal and mediolateral oblique projections were averaged: average distance = [(craniocaudal distance + mediolateral oblique distance)/2], creating the average distance off target for the initial deployment of the marker clip. The average distance off target in this context is a measurement of the marker clip distance from the target lesion center. Since two deployment methods were used in this study, the average distance off target was analyzed according to deployment method.

Stability of Marker Clip Placement Over Time

In the second context, the stability of marker clip placement over time was measured by comparing the position of the marker clip on the craniocaudal and mediolateral oblique masks immediately after biopsy and marker clip deployment to the position of the marker clip on craniocaudal and mediolateral oblique mammograms obtained at first imaging follow-up. As before, the skin outlines from the mammograms obtained at first imaging follow-up were fitted to the craniocaudal and mediolateral oblique masks by using the nipple as the fulcrum to create the best fit between each follow-up mammogram first imaging follow-up mammogram and the corresponding mask.

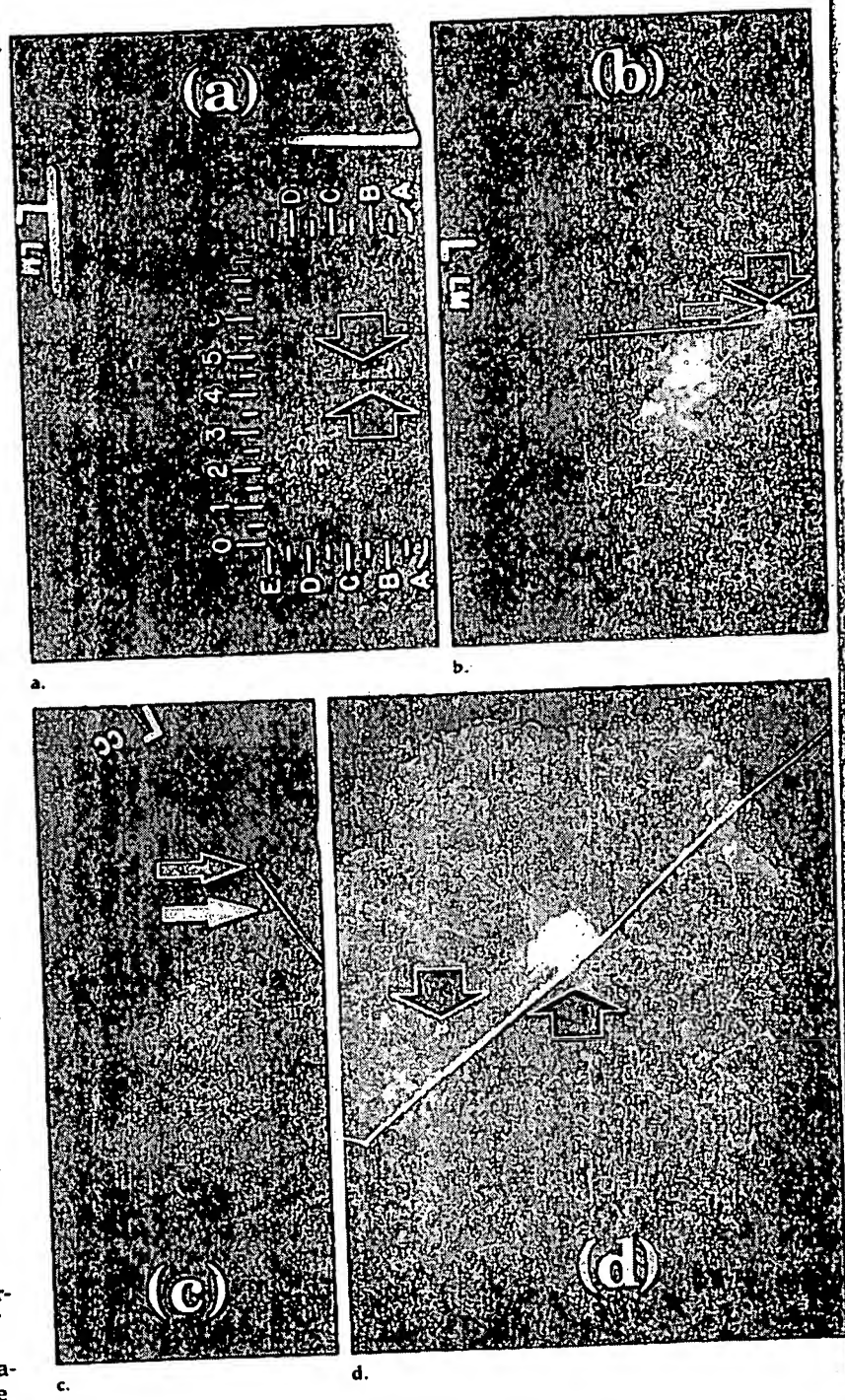


Figure 3. Photographs of mammograms show the steps necessary to use a marker clip as a target for wire localization before surgery. Wire localization was performed in the same lesion shown in Figure 2. (a) Lateromedial mammogram obtained with an alphanumeric grid placed over the left breast in the lateromedial projection. Wax pencil lines have been drawn on the lateromedial mammogram grid over the region of residual target lesion (upward-pointing arrow) just adjacent to the marker clip (downward-pointing arrow). A stiffened localization wire (Kopans Spring Hookwire; Cook, Bloomington, Ind) was then placed where the wax pencil lines cross in the lateromedial projection. (b) Lateromedial mammogram helps verify the position of the localization wire. The black arrow highlights the marker clip; the gray arrow highlights a "BeBe" (Beekley Spots with Pik-Up; Beekley Corporation, Bristol, Conn), which has been placed at the skin entry site of the wire. (c) Craniocaudal mammogram shows the position of the localization wire, the marker clip (white arrow), and the skin BeBe (gray arrow). (d) Magnified (×2) radiograph of the surgical specimen cut and compressed in a plastic transportation and compression container (TranSpec; E-Z-Em, Westbury, NY) shows the residual target lesion (upward-pointing arrow), the marker clip (downward-pointing arrow), and the localization wire. The marker clip has been moved away from the target lesion with surgical transection of the specimen and pressure from the plastic compression container.

Of 149 marker clips placed, 36 (24%) patients subsequently underwent surgical therapy. At stereotactic biopsy, infiltrating breast cancer was diagnosed in 20 (56%) of the 36 lesions, ductal carcinoma in situ in 13 (36%) lesions, and atypical ductal hyperplasia in three (8%) lesions. The type of surgery performed, whether the marker clip was used as a guide for wire localization, whether a radiograph was obtained of the surgical specimen, and the distribution of histologic diagnoses are summarized in Table 4.

In eight (22%) of the 36 lesions, no preoperative wire localization was performed. Seven of the eight surgeries were mastectomies and the other surgery was breast-conserving surgery directed by palpation of a hematoma presumed by the surgeon to be at the directional, vacuum-assisted breast biopsy site. In 10 (28%) of the 36 lesions, the marker clip was used as the target for wire localization. However, no radiograph was obtained of the specimen because the biopsy site was readily visible during surgery and radiography was deemed redundant by the surgeon. In 18 (50%) of the 36 lesions, the marker clip was used as the target for wire localization and a radiograph was obtained of the specimen. On all 18 (100%) of these radiographs, the marker clip and the previous biopsy site were identified positively in the specimen.

In 29 (81%) of the 36 lesions, the biopsy site and residual tumor were identified positively at histopathologic examination. In the remaining seven (19%) lesions, the biopsy site was also identified positively, and the pathologist concluded that the target lesion had been excised with clear margins at directional, vacuum-assisted breast biopsy before wire localization and surgical therapy. No evidence of tumor seeding or epithelial displacement was identified in any of the 36 surgical specimens (13).

DISCUSSION

With use of 14-gauge and 11-gauge directional, vacuum-assisted breast

Table 1

Comparison of 14- and 11-gauge Directional, Vacuum-assisted Probes according to Specimen Weight, Specimen Number, Lesion Diameter, and Percentage of Excisional Biopsies

Probe Size	No. of Biopsies	Average Aggregate Weight (mg)*	Average No. of Specimens Obtained†	Average of Individual Weights per Specimen (mg)‡	Average of Mean Lesion Diameters (mm)§	Excisional Biopsies (%)‖
14	49	1,171	27	44	9.1	59
11	100	1,949	19	105	7.8	79

* Weights were determined in the pathology department. $P \leq .0001$ (unpaired t test).
† $P \leq .0001$ (unpaired t test).
‡ $P \leq .0001$ (unpaired t test).
§ $P \geq .13$ (unpaired t test); no statistically significant difference in measurements.
‖ $P \leq .03$ (unpaired t test).

Table 2

Analysis of Variance of Average Distance off Target according to Count, Mean, Standard Deviation, and Standard Error

Independent Variables	Count	Mean	Standard Deviation	Standard Error
Benign control lesions	22	7.7	3.8	0.8
Deployment method				
13-gauge straight needle	43	12.6	12.3	1.9
11-gauge through probe	106	12.6	7.2	0.7
First imaging follow-up	31	8.7	4.4	0.8

Table 3

Overall Results of Analysis of Variance

	df	Sum of Squares	Mean Square	F Value	*P* Value
Independent variables ($n = 4$)	3	744	248	3.9	≤.01
Residual	198	12,616	64	...	...

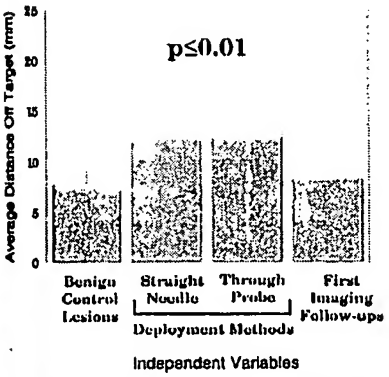


Figure 4. Bar graph shows the plotted average distance off target for each of the four independent variables. Thin bars define the 95% confidence intervals.

biopsies, it is the clinical goal to perform a diagnostic percutaneous breast biopsy as completely and accurately as imaging-guided wire localization and open surgical breast biopsy. With the current directional, vacuum-assisted probes, the goal is not to perform therapeutic breast surgery percutaneously. However, to perform a complete diagnostic breast biopsy, "enough" breast tissue must be obtained percutaneously in all breast lesions. "Enough" tissue may be more tissue than many radiologists are accustomed to removing.

We believe that when stereotactic targeting is nearly perfect, the volume of tissue described in Table 1 for 14-gauge probes is just sufficient to consistently perform a complete and accurate diagnostic breast biopsy. Furthermore, we believe that the volume of tissue obtained with the 11-gauge probe (Table 1) may be sufficient to compensate for small stereotactic targeting errors that occur occasionally. Consequently, we now perform only 11-gauge directional, vacuum-assisted breast biopsies.

Data are available in the literature for atypical ductal hyperplasia and ductal carcinoma in situ lesions that clearly support our first belief. When the diagnosis of atypical ductal hyperplasia is ascertained at percutaneous breast biopsy and surgery is performed subsequently and ductal carcinoma in situ or infiltrating breast cancer is identified at the biopsy site within the surgical specimen, the degree of disease in the breast has been underestimated at percutaneous biopsy (14). Similarly, if ductal carcinoma in situ is identified at percutaneous breast biopsy and infiltrating breast cancer is later identified at surgery, the degree of disease in the breast has been underestimated at percutaneous biopsy (14). When 14-gauge, automated core needle breast biopsies are performed, with acquisition of five to eight specimens per lesion, rates of underestimation of atypical ductal hyperplasia and ductal carcinoma in situ are high, approximately 50% and 20%, respectively (15–17). Even when 17 to 19 specimens are obtained with 14-gauge, automated core needle biopsy, the rate of underestimation of atypical ductal hyperplasia decreases only to 44% and that of ductal carcinoma in situ decreases only to 16% (14).

When 16 or 17 specimens are obtained with 14-gauge, directional vacuum-assisted biopsy, the rate of underestimation of atypical ductal hyperplasia decreases to 18% and the rate of underestimation of ductal carcinoma in situ decreases to 9% (18), (unpublished data). Although these rates are improved compared with rates of underestimation associated with 14-gauge automated core needle biopsies, underestimation of disease at the biopsy site still exists.

To eliminate underestimation of atypical ductal hyperplasia and ductal carcinoma in situ, approximately 30 specimens must be obtained from each lesion with 14-gauge directional, vacuum-assisted biopsy (14). At this level of percutaneous tissue acquisition, over 1 g of tissue is obtained (Table 1). Furthermore, when we use the 11-gauge directional, vacuum-assisted probes, nearly 2 g of tissue are removed at the biopsy site (Table 1).

When over 1 g of tissue is removed from lesions in which the average diameter is 1 cm or less, all mammographic signs of the lesion may be removed as well. If fact, for small lesions (5 mm in diameter or less), we expect to remove all visible signs of the lesion during the directional, vacuum-assisted breast biopsy. The marker clip was developed to ensure that a target would still be present for subsequent wire localization and therapeutic surgery.

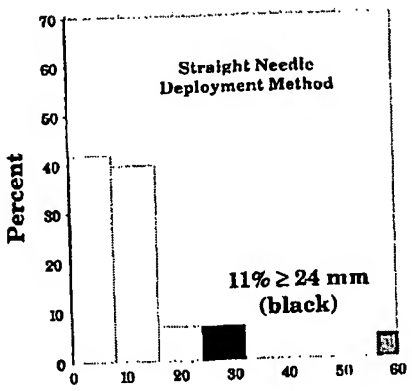
Our study demonstrates that on average, the marker clip was deployed about 5 mm from the center of the target lesion (12.6 mm − 7.7 mm = 4.9 mm). Since the average lesion diameter for the 149 marker clip placements was approximately 10 mm, the overall accuracy of deployment was good. On average, the marker clips were placed just outside the margin of each lesion. Although no clinical problems were encountered from any of the marker clip deployments in our study, there were potential clinically meaningful exceptions to this general rule. In 11% of the straight-needle deployments and 7% of the through-probe deployments, the average distance off target was 24 mm or more. An average distance off target of 24 mm or more could potentially lead to a clinical problem at wire localization and therapeutic surgery. We could not predict from the manipulation of the marker clip deployment system when an off-target deployment had occurred. We were aware of off-target placements only as we examined the two-view mammograms obtained immediately after biopsy.

If the position of the marker clip with respect to the target lesion is known immediately after placement of the marker clip, a deployment error of 24 mm or more would not necessarily lead to a clinical problem. If the position of the marker clip with respect to the target lesion is known, then any error in deployment of the marker clip can be taken into account at wire localization and surgery. However, if the position of the marker clip with respect to the target lesion is not known and the average distance off target is large, then a clinical problem might occur. This clinical problem may occur particularly if the patient underwent stereotactic biopsy and marker clip placement at one site and wire localization and surgery were performed at another. At the second site, it might be assumed incorrectly that the marker clip was exactly on target. Consequently, we believe it is important to document the position of the marker clip after each deployment with a standard two-view, upright mammogram. This two-view upright mammogram should then become a part of the patient record and be available for review before wire localization is performed.

We do not believe it is sufficient to repeat stereotactic mammography while the patient is still on the biopsy table and to use the stereotactic mammogram to measure deployment accuracy. It is possible to calculate the x, y, and z coordinates of the marker clip from a repeat stereotactic mammogram. However, the coordinates calculated may give the operator a false sense of security, since in compression the coordinates of the marker clip are almost always close to the coordinates of the center of the target lesion. Because of the accordion-like character of the breast with bands of tough fibrous tissue alternating with bands of softer, fatty tissue, this method of documenting marker clip position is not reliable. The marker clip may attach to a band of fibrous tissue that in compression is close to the center of the target lesion but when the clip is out of compression it is at some distance from the center of the lesion. To avoid this pitfall, the stereotactic mammograms should be used only to document that the marker clip was deployed. To determine where the marker clip was deployed, upright standard mammography is necessary.

Our study also demonstrates that the marker clip did not change position over the follow-up period of the study (mean, 8.6 months). The average distance off target for marker clip measurements at first imaging follow-up were not statistically significantly different from the average distance off target measurements for the benign control lesions. Therefore, once the location of the marker clip is documented with upright mammography after deployment, it can be safely assumed that the marker clip will remain where deployed for at least 8.6 months. Stability over longer periods has not been documented, to our knowledge.

Marker clip misplacements (average off target distance > 24 mm) were more frequent when the straight-needle deployment method was used than when the through-probe deployment method was used (11% vs 7%, not statistically significant). Furthermore, the straight-needle deployment method necessitated more deployment steps than were necessary for



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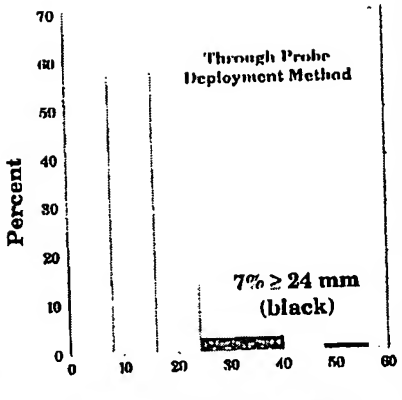

6.

Figures 5, 6. Graphs show the percentage distribution of the average distance off target for the (5) straight-needle deployment method and the (6) through-probe method. The white bars represent an average distance off target of less than 24 mm; the black bars represent an average distance off target of 24 mm or greater. For the straight-needle deployment method, 11% of the average distance off target measurements were 24 mm or greater, and for the through-probe method, 7% of the average distance off target measurements were 24 mm or greater.

Table 4
Type of Surgery Performed and Histologic Diagnosis in 36 Lesions

Surgery Performed	Metallic Clip Used for Localization	Radiograph Obtained of Surgical Specimen	Histologic Diagnosis			
			Infiltrating Breast Cancer	Ductal Carcinoma In Situ	Atypical Ductal Hyperplasia	Total*
Mastectomy	No	No	4	3	0	7 (19)
Breast conserving	No	No	1	0	0	1 (3)
Breast conserving	Yes	No	6	3	1	10 (28)
Breast conserving	Yes	Yes	9	7	2	18 (50)

* Numbers in parentheses are percentages.

the through-probe method, more time was necessary to perform the straight-needle method because of the greater number of steps, and the straight needle is no longer available from the manufacturer. Consequently, we currently perform only through-probe deployments.

The marker clip was a successful guide for wire localization before surgery. In all 18 cases in which the marker clip was used as a surrogate for the target lesion for wire localization before surgery, the marker clip and the biopsy cavity were identified in each of the 18 surgical specimens.

The mask measurement system for defining the position of the lesion and the marker clip on one image was developed specifically for this study. However, we soon observed that other radiologists who performed wire localization at our center were pulling the masks from the research files at wire localization to analyze the masks before placement of a localization wire. The masks contain all the information necessary to use the marker clip as a reference point at wire localization regardless of whether the marker clip is exactly on target. Consequently, we continue to create a set of masks for each marker clip deployed from mammograms obtained before and after biopsy and marker deployment.

The most common question asked by patients before signing consent for placement of a marker clip was in regard to the size of the clip being placed in the breast. We initially used a small air gap between our thumb and index finger to show marker clip size and informed the patients that the clip was 2 mm. However, this communication method was not very effective, as most patients did not think in terms of millimeters and the space between index finger and thumb was a crude approximation of clip size. To overcome this communication gap, we attached an actual marker clip to an exposed (black) sheet of x-ray film. Against this black background, the marker clip is clearly visible. Once the size of the marker clip was seen, the patients generally expressed no further concern about having the marker clip placed permanently in the breast. We keep the marker clip sample pinned to the wall in the stereotactic breast biopsy room and find it a useful communication aid to obtain informed consent.

Before we used the marker clip, we were able to perform wire localization successfully in all lesions in which stereotactically guided biopsy was performed and surgery was necessary. In small lesions, however, we had a degree of concern with regard to the time between stereotactic biopsy and wire localization. We were particularly concerned when a patient was to be transferred to another facility for wire localization and definitive breast cancer surgery. In the hope that residual blood or air might remain at the biopsy site to identify the biopsy site if the target lesion were removed entirely at stereotactic biopsy, we attempted to minimize the time from stereotactic biopsy to wire localization. This source of concern has now been eliminated. Because of the marker clip, we are now confident that wire localization can be performed successfully at any time after stereotactic breast biopsy whether residual blood or air from the biopsy are present at wire localization.

Finally, with the availability of the marker clip, it is not necessary to place lower size limits on lesions that can undergo stereotactic biopsy. For small lesions (< 5 mm in diameter), we anticipate that in a high percentage of cases all visible signs of the target lesion will be removed. However, because a marker clip is placed after each stereotactic biopsy of these smaller lesions, we are confident that the biopsy site can be reached accurately at wire localization with the marker clip as the surrogate target. Furthermore, even when a marker clip is off target, knowledge of the direction and magnitude of the deployment error allows the marker clip to be used as a clear-cut point of reference for wire localization. ■

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Clip Migration after 11-gauge Vacuum-assisted Stereotactic Biopsy: Case Report[1]

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Index terms:
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Foreign bodies, 00.93

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A 68-year-old woman underwent stereotactic biopsy of a small cluster of calcifications. The postbiopsy mammograms showed the biopsy-marking clip to be located correctly at the biopsy site. Follow-up mammograms 1 year later showed that the clip migrated to another quadrant of the breast. Findings in this case demonstrate that at long-term follow-up a biopsy-marking clip may not be accurately marking the biopsy site.

Biopsy-marking clips ideally should mark biopsy sites accurately. However, incorrect location of the clip immediately after biopsy can occur owing to the "accordion effect." In the case we report here, findings showed that the clip migrated after the immediate postbiopsy period. Since clip migration can affect interpretation of mammographic findings and localization for future surgery, the radiologist should not assume that the clip is correctly located at the biopsy site. The radiologist should compare prebiopsy, postbiopsy, and follow-up mammograms to determine whether the biopsy-marking clip has moved.

Case Report

We received approval from our Human Investigation Committee for Medical Record Review; informed consent was not required.

At mammography, a 68-year-old woman had a small cluster of calcifications at the 10- to 11-o'clock position in the posterior third of the right breast. Stereotactic core biopsy was performed from a superior approach in the craniocaudal projection with an 11-gauge vacuum-assisted suction device (Mammotome; Biopsys/Ethicon-Endosurgery, Cincinnati, Ohio). Since most of the calcifications were removed, a biopsy-marking clip (MicroMark; Biopsys/Ethicon-Endosurgery) was deployed. Our method of clip deployment is to withdraw the probe 3–5 mm, to insert the introducer, and to deploy the clip while the vacuum is simultaneously applied. The postprocedural digital stereotactic images demonstrated the presence of the clip in the air-filled biopsy cavity. The postbiopsy craniocaudal and mediolateral mammograms showed the clip accurately located at the site where samples of calcifications were removed (Fig 1). There were no complications. In particular, no excessive bleeding occurred during the biopsy. The histologic results were benign.

At routine mammographic follow-up 1 year later, a small scar at the biopsy site and a few residual calcifications were noted (Fig 2). The biopsy-marking clip, however, was no longer located at the biopsy site but was in the inferior aspect of the breast. Since the clip was at the correct site following the procedure, migration must have occurred at some time after the postprocedure mammograms were obtained.

Discussion

The use of the 11-gauge vacuum suction device can result in complete removal of a mammographic abnormality. For small lesions, a biopsy-marking clip is available to localize the site of biopsy for subsequent surgery if necessary. While findings reported in articles (1–5) about this procedure have shown the clip to be in close proximity to the biopsy site in the majority of cases, it is known that the final location of the clip can be at remote

Author contributions:
Guarantors of integrity of entire study, L.E.P., C.H.L.; study concepts and design, L.E.P.; literature research, L.E.P.; clinical studies, L.E.P.; data acquisition and analysis/interpretation, L.E.P.; manuscript preparation, L.E.P., C.H.L.; manuscript definition of intellectual content, L.E.P.; manuscript editing, revision/review, and final version approval, L.E.P., C.H.L.

Exhibit L

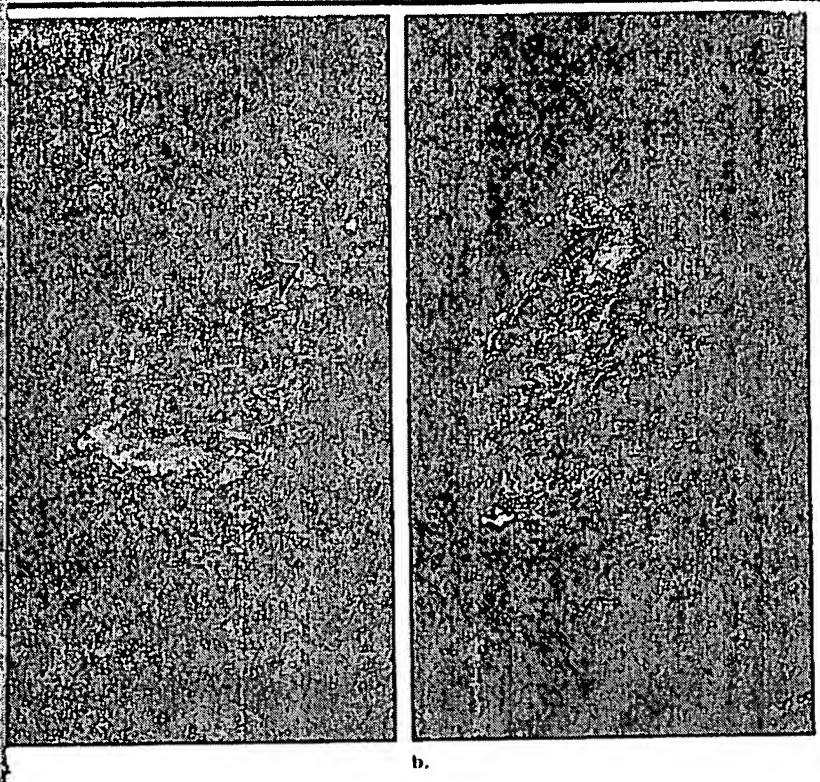

Figure 1. (a) Craniocaudal and (b) mediolateral postprocedural mammograms show the clip (arrow) accurately located at the biopsy site. Almost all of the calcifications were removed. Results of histologic analysis showed that the calcifications were benign.

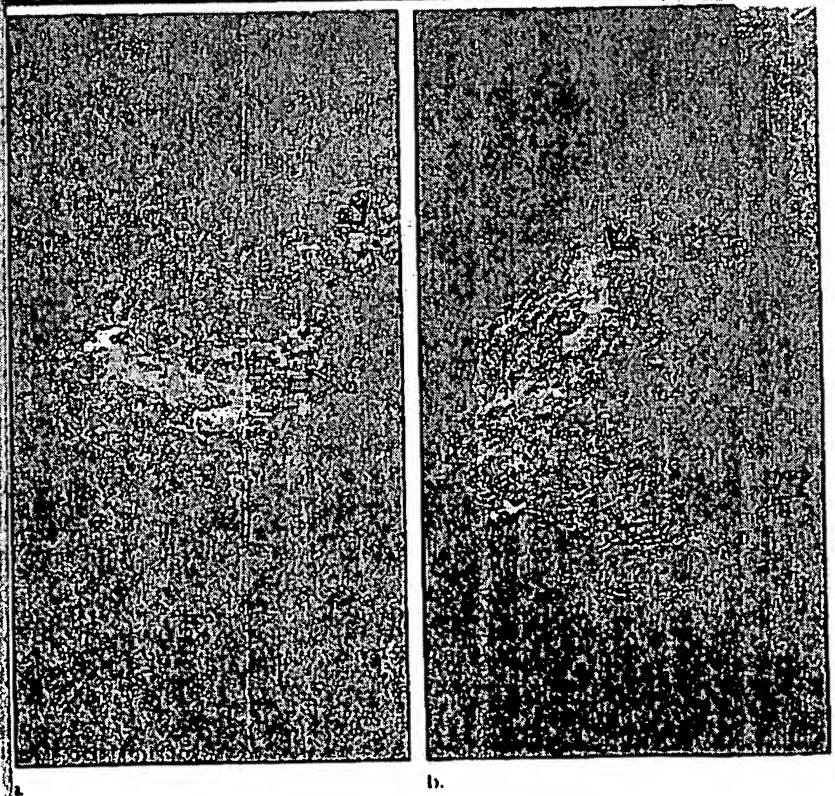

Figure 2. (a) Craniocaudal and (b) mediolateral oblique images obtained 1 year after the biopsy show the clip (solid arrow) in the inferior aspect of the breast. A small scar and a few residual calcifications are at the previous biopsy site (open arrow).

sites, several centimeters or more from the area of sampling in some cases. Since the clip is deployed at the termination of the stereotactic procedure while the breast remains in compression, release from compression can result in a change in the location of the clip to a position either proximal or distal to the biopsy cavity, along the z axis of the needle track (accordion effect). Furthermore, if the clip is not firmly attached to breast tissue when deployed, bleeding can cause the clip to travel through the needle track and even out of the breast (6). For these reasons, postprocedural mammograms are advocated to document the relationship of the clip to the biopsy site (4).

In this case, although the postbiopsy mammograms showed the clip to be located correctly at the site where samples of calcifications were removed, subsequent mammograms 1 year later revealed the clip to be markedly displaced. The exact mechanism and timing of the displacement are not known. On review of the digital image obtained after clip deployment, the clip was in a dependent portion of the cavity, possibly indicating poor adherence to tissue. Applying the vacuum suction while the clip is deployed should, theoretically, allow the clip to adhere to tissue rather than to be free floating in the biopsy cavity. Despite good technique, however, the clip may not always be firmly attached. Although there was no hematoma formation or history of postprocedural bleeding in this case, it is possible that the clip migrated within the patent needle track soon after the procedure.

An alternative explanation is that the clip freely migrated within the predominantly fatty tissue of the breast. Wires used for needle localization prior to surgery have been reported (7,8) to migrate within the breast and to remote areas of the body. If the case presented here represents similar migration, then biopsy-marking clips may have the potential to migrate some distances within or away from the breast.

Burbank and Forcier (3) have shown long-term stability (mean follow-up time, 8.6 months) of the localizing clip in 31 cases. No measurable movement over time was noted. Longer follow-up times have not been reported. Findings in our case demonstrate that clip migration after postbiopsy imaging is possible, and the position of the clip on subsequent mammograms, therefore, may not be accurate and reliable for future documentation of the biopsy site. This has important implications for subsequent localization for surgery and for interpretation of follow-up mammograms. Radiologists who perform needle localizations or who interpret mammograms after stereotactic core biopsies in which a clip was placed should not assume that the clip is in the correct location and should always review prebiopsy mammograms.

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Metallic Clip Deployment during Stereotactic Breast Biopsy: Retrospective Analysis[1]

PURPOSE: To determine the visibility of presumably excised lesions on screen-film mammograms obtained after biopsy and to determine the accuracy of clip deployment on the basis of measurements obtained on routine pre- and postbiopsy mammograms.

MATERIALS AND METHODS: One hundred eleven cases of core-needle biopsy with clip deployment were reviewed. In each, the type of lesion, lesion location, and biopsy approach were recorded. Pre- and postbiopsy images were reviewed, and the distance between the clip and biopsy site was measured. Postbiopsy images were reviewed to determine whether the targeted lesion remained visible.

RESULTS: In 62 (56%) cases, the clip was located within 5 mm of the target on postbiopsy images (craniocaudal and mediolateral), while in 18 (16%), the clip was within 6–10 mm on one projection. However, 31 (28%) clips were more than 1 cm from the target on at least one postbiopsy image. Of the 111 cases, 39 (35%) were malignant or atypical and required excision. Of these, 18 (46%) had clips at least 1 cm from the targeted lesion on at least one projection.

CONCLUSION: Metallic clips placed during core-needle breast biopsy are intended to mark the biopsy site when the visible lesion is excised, in case additional biopsy is required. The data suggest that the position of metallic clips placed during stereotactic core-needle biopsy may differ substantially from the location of the biopsy site. Postbiopsy mammography should be performed in two orthogonal planes to document clip position relative to the biopsy site.

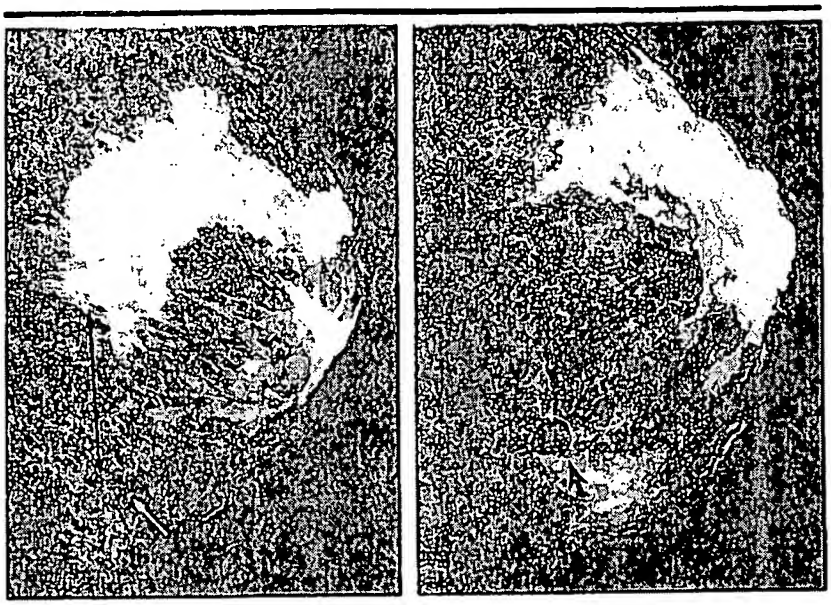
One of the main advantages of vacuum-assisted biopsy needles is their ability to obtain larger volumes of tissue per sample compared with spring-activated needles (Baxter Healthcare, Valencia, Calif). Larger tissue samples improve the core-biopsy technique by reducing volume-sampling errors. One anticipated sequela of larger samples, however, is that small lesions may not be visible after biopsy (1–3). To overcome this potential limitation, stainless steel clips are often deployed at the completion of stereotactic breast biopsy to localize the biopsy site when the targeted lesion has been excised, in case additional surgery is required.

However, determination of whether a lesion is still visible after biopsy is often difficult, especially when this assessment is based solely on the digitally acquired images obtained during biopsy. This difficulty results because the digital images are obtained with limited compression, because orthogonal images cannot be obtained, and because the lesion may be partially obscured by hematoma. Therefore, it is possible that these clips are being deployed when the lesion has not been completely removed, and the residual target is visible only on dedicated screen-film mammograms obtained immediately after biopsy.

The main reason for deploying a clip is to provide a visible marker at the site of the excised biopsy target so that needle localization can be performed if indicated. To be effective, the clips must be deployed at the intended site and must remain close. However, there are limited published data on the deployment accuracy of these clips. In two separate studies, Liberman et al (4) and Reynolds (5) reported clip placement accuracy, as determined by comparing the coordinates of the clip and those of the original target on the stereotactic images. Burbank and Forcier (6) alternatively determined their initial clip placement accuracy on the basis of the mask measurement system by using mammograms obtained before and after biopsy.

Author contributions:
Guarantor of integrity of entire study, E.L.R.; study concepts and design, E.L.R.; definition of intellectual content, E.L.R.; literature research, E.L.R., T.T.V.; clinical studies, E.L.R., T.T.V.; data acquisition and analysis, E.L.R., T.T.V.; statistical analysis, E.L.R., T.T.V.; manuscript preparation, editing, review, and final version approval, E.L.R., T.T.V.

Exhibit M



a. b.

Figure 1. Example of clip-to–biopsy site measurement on postbiopsy mammograms. Stereotactic vacuum-assisted biopsy of the original cluster of indeterminate microcalcifications in the lower inner quadrant of the left breast (not shown) was performed with an inferior approach. (a) The targeted lesion was excised, and an air-containing cavity (single-headed arrow) is depicted at the biopsy site on the postbiopsy mediolateral projection. The metallic clip is displaced cephalad. Clip displacement was determined by the distance (double-headed arrow) between the center of the original lesion and the clip along a line parallel to the plane of compression. (b) On the craniocaudal mammogram, the metallic clip is deployed within 5 mm from the biopsy site (arrow).

It has been demonstrated that the clips can be deployed near the biopsy site initially, while the patient's breast is compressed. However, as the compression is released, small discrepancies between the clip and the biopsy site may become magnified (the accordion effect), particularly in the plane perpendicular to the plane of compression used during stereotactic core-needle biopsy (4,6). Thus, small differences, as measured on postbiopsy digitally acquired stereotactic views, may result in substantial underestimation of the distance between the clip and the biopsy site on the orthogonal view. Such a discrepancy could limit the ability to accurately localize the correct area for subsequent surgery.

Because preoperative needle localization of lesions previously evaluated at biopsy with stereotactic guidance is often performed mammographically, the purpose of this study is twofold. First, this study was undertaken to determine the visibility of presumably excised lesions on postbiopsy screen-film mammograms. Second, it was undertaken to determine clip deployment accuracy on the basis of measurements obtained from routine pre- and postbiopsy mammograms.

MATERIALS AND METHODS

Between November 1, 1997, and June 30, 1999 (20 months), 258 consecutive patients were referred to our institution for stereotactic vacuum-assisted breast biopsy of mammographically suggested lesions. In all cases, biopsy was performed with a dedicated prone unit with digital imaging (StereoGuide; LoRad, Danbury, Conn) and a vacuum-assisted biopsy system with an 11-gauge biopsy probe (Mammotome; Biopsys Medical, Irvine, Calif). A minimum of six specimens were obtained from each lesion. The decision to obtain additional specimens was based on the size of the lesion, results of the specimen radiographs in cases of microcalcifications, and findings on the stereotactic images.

After biopsy, the biopsy needle was retracted at least 5 mm from the biopsy position, and a pair of stereoradiographs was obtained to determine if the mammographic lesion was excised. The stereoradiographic images were optimized by adjusting the window and level settings and by using one of the sharpening filter algorithms provided by the manufacturer for use in cases of microcalcifications. On the basis of the findings at final assessment of the stereotactic images, a marker clip was placed at the discretion of the radiologist performing the procedure. For microcalcifications, criteria for clip deployment were that the postbiopsy stereo images did not demonstrate residual microcalcifications. For masses and focal asymmetric densities, criteria for clip placement included lack of visualization of the targeted lesion due to removal or obscuration by hematoma.

In 111 (43%) of the 258 stereotactic vacuum-assisted biopsies, a tissue marker (MicroMark II; Biopsys Medical, Irvine, Calif, or Site Marker Clip; US Surgical, Norwalk, Conn) was deployed at the conclusion of the biopsy procedure to radiographically mark the location of the biopsy site. These cases constituted our study population. In all 111 cases, the marker clip was positioned at the biopsy site by using the through-probe technique (7), as described in the instruction manual.

Following clip placement, a pair of stereotactic images was obtained to confirm clip deployment. In addition, final mammographic images were also obtained in at least two projections, craniocaudal and mediolateral oblique, to verify placement and accuracy. If a prebiopsy mediolateral view was available, a corresponding postbiopsy mediolateral projection was also obtained. If a discrepancy was present between the clip and the biopsy site, it was recorded at the time of biopsy.

A retrospective review of the pre- and postbiopsy mammograms of the 111 cases of stereotactic breast biopsy with clip deployment was performed. For all cases, the type of lesion (ie, mass, density, architectural distortion, or microcalcifications), lesion size, number of cores obtained, and the biopsy approach (ie, superior or inferior or lateral or medial) were recorded. In addition, the lesion location was recorded, either by clock position or quadrant, to confirm the site of the lesion on postbiopsy mammograms.

Postbiopsy images were then examined to determine if the targeted lesion was excised, obscured by hematoma, or remained visible. The clip-to–biopsy site distance (defined as the distance from the center of the target to the clip in a line parallel to the plane of compression) was measured on craniocaudal and mediolateral oblique projections by consensus of two radiologists (T.T.V., E.L.R.).

Measurements were performed by aligning the prebiopsy craniocaudal and mediolateral oblique images with the corre-

sponding postbiopsy images by using parenchymal and soft-tissue landmarks (eg, nipple, pectoralis muscle, and vascular structures). If the mammographic lesion was identified on postbiopsy images, a line parallel to the plane of compression was drawn from the center of the expected lesion to the clip, and the distance was recorded. If the lesion was seen as being excised on the postbiopsy images but if the biopsy cavity was filled with air and/or if a hematoma was identified, the line was then drawn between the center of the biopsy cavity and the clip (Fig 1). If neither the mammographic lesion nor the biopsy cavity was visible, the circumference of the original lesion was outlined on the prebiopsy craniocaudal and mediolateral oblique images by using a wax marker.

The corresponding postbiopsy image was superimposed on the prebiopsy image to allow the outline of the lesion to be shown through the postbiopsy mammogram. By using the outline of the lesion as the reference, the distance between the expected center of the lesion and the clip was then measured. The accuracy of clip placement was determined by determining the position of the clip relative to the mammographic lesion and was recorded as 5-, 6–10-, 11–19-, or >20-mm displacement from the center of the targeted lesion.

Each lesion was retrospectively correlated with the histopathologic diagnosis (categorized as benign, infiltrating breast carcinoma, ductal carcinoma in situ, or atypical hyperplasia). If presurgical needle localization was performed, the needle localization images and surgical specimen radiograph were also reviewed. All presurgical needle localizations procedures were performed by using an alphanumeric grid and a needle–hook wire system to localize the metallic clip and the residual lesion (if visible).

In general, the same plane of compression used for core-needle biopsy was used for needle localization. If there was a large discrepancy between the location of the clip and the targeted lesion on the postbiopsy images, both were localized separately. All surgical specimens were imaged at the time of surgery to confirm that the targeted lesion and the marker clip were excised. Furthermore, in all cases involving definitive surgery, the surgical histopathologic findings were also reviewed to ensure mammographic-pathologic correlation.

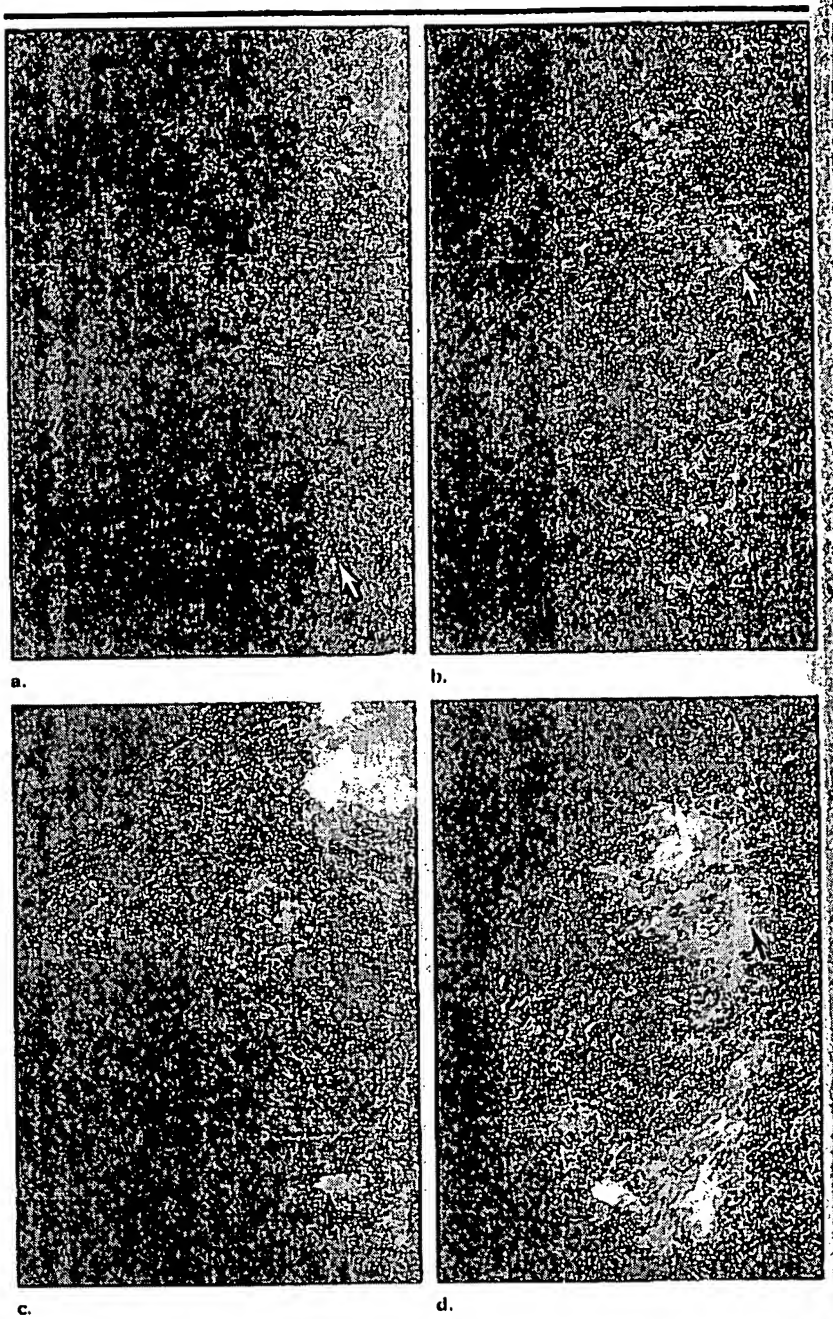


Figure 2. Accurate clip placement on two orthogonal views. On prebiopsy (a) craniocaudal and (b) mediolateral views, the palpable abnormality (indicated by the radiopaque BB marker) at the 2-o'clock position in the right breast corresponds to a partly obscured, noncalcified, oval mass (arrow). Stereotactic vacuum-assisted biopsy was performed from a superior approach. Pathologic analysis revealed fibroadenoma. Postbiopsy (c) craniocaudal and (d) mediolateral mammograms demonstrate hematoma and air at the biopsy site (arrow). The metallic clip is within 5 mm of the biopsy site on both projections.

RESULTS

Mammographic findings of the 111 lesions were characterized as clustered microcalcification in 79 (71%), masses in 28 (25%), architectural distortion in two (2%), and developing asymmetric densities in two (2%). The mean lesion size

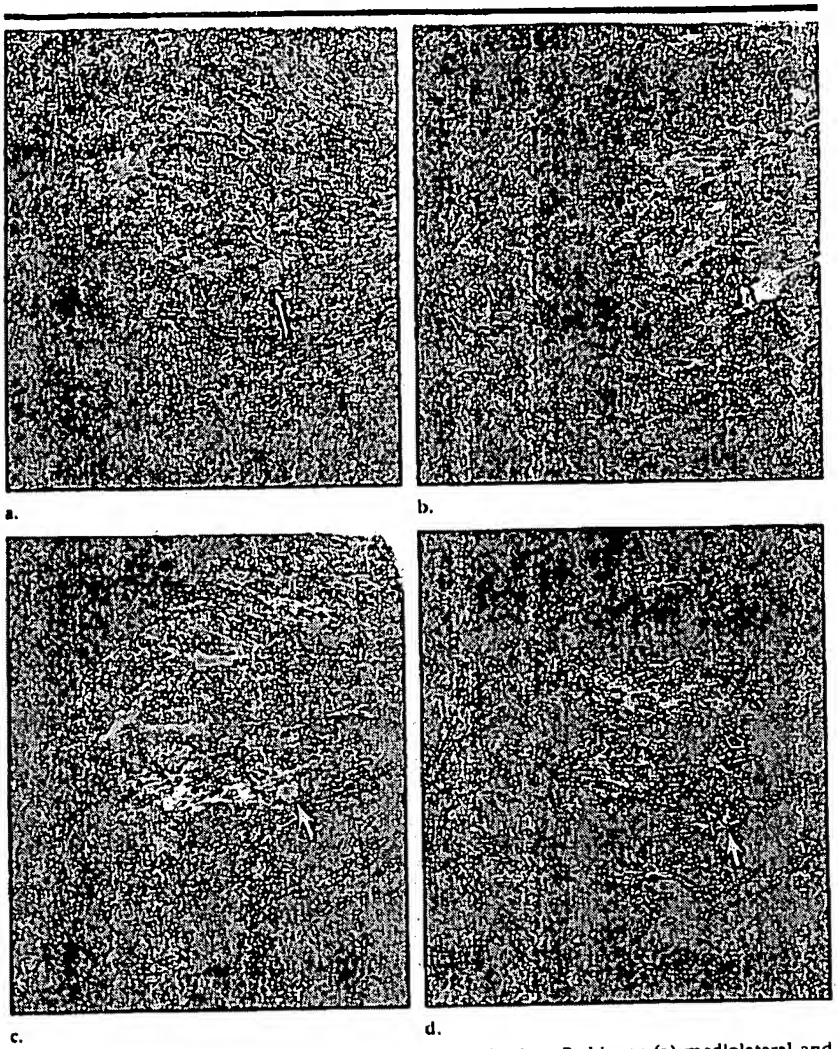


Figure 3. Metallic clip displacement on only one projection. Prebiopsy (a) mediolateral and (b) craniocaudal mammograms show an obscured lobulated mass (arrow) in the central right breast. Stereotactic vacuum-assisted biopsy was performed with a medial approach, with the breast in mediolateral compression. The mammographic lesion was obscured by hematoma on postbiopsy stereotactic images (not shown). A metallic clip was subsequently deployed to mark the biopsy site. Pathologic analysis revealed fibroadenoma. (c) In retrospect, a residual mass (arrow) is evident on the postbiopsy mediolateral mammogram. The metallic clip is within 5 mm of the biopsy site. (d) Craniocaudal mammogram of the right breast obtained immediately after stereotactic biopsy shows a small hematoma at the biopsy site (solid arrow). The clip (open arrow) is displaced 25 mm lateral to the biopsy site. The displacement is only in this plane, which is perpendicular to the plane of compression at stereotactic biopsy.

was 7.8 mm (range, 2–23 mm). In 61 (55%) of 111 lesions, biopsy was performed with craniocaudal compression for either a superior or inferior approach. In 50 (45%) of 111 lesions, biopsy was performed with lateral compression for a medial or lateral approach. The mean number of specimens obtained was 10.7 cores (range, 6–27 cores). In the 111 lesions in which a marker clip was deployed, the histopathologic findings were benign in 72 (65%), malignant in 26 (23%), and atypical hyperplasia in 13 (12%). Of the 26 malignant lesions, infiltrating breast carcinoma was diagnosed in eight, and ductal carcinoma in situ was diagnosed in 18.

Retrospective review of the mammographic images obtained after clip deployment demonstrated that 28 (25%) of 111 lesions remained partially visible on postbiopsy images. Of the 28 lesions that were mammographically visible after clip placement, 14 (50%) were benign, one (4%) was atypia, 10 (36%) were invasive carcinoma, and three (11%) were ductal carcinoma in situ. In 83 (75%) of the 111 lesions examined at biopsy, the original lesion was completely removed or obscured by hematoma.

In our study, the distance from the clip to the center of the original lesion was within 5 mm on both craniocaudal and mediolateral oblique projections in 62 (56%) of the 111 cases in which marker clips were placed (Fig 2). Clip placement in 40 of these 62 cases was performed with craniocaudal compression, and clip placement in 22 cases was performed with lateral compression. In the 111 cases, the clip-to-lesion distance on at least one projection was 6–10 mm in 18 (16%) and greater than 10 mm in 31 (28%) (Fig 3). In 31 cases, the clip was more than 1 cm away from the targeted lesion on at least one projection. In 16 cases, it was 10–20 mm away; in seven, 20–30 mm away; and in eight, more than 30 mm away.

Tables 1 and 2 show the accuracy of clip deployment on at least one craniocaudal and mediolateral oblique projection at biopsy performed with craniocaudal and lateral compression. Our data suggest that the largest error occurred in the plane orthogonal to the compression plane used for the percutaneous biopsy (z axis). In 61 biopsies performed with craniocaudal compression, 60 (98%) clips were within 1 cm of the lesion examined at biopsy, one (2%) was 1–2 cm from the lesion, and no clip was more than 2 cm from the lesion on the postbiopsy craniocaudal projections.

However, on the postbiopsy mediolateral oblique mammograms, eight (13%) of 61 clips placed with craniocaudal compression were more than 2 cm from the biopsy site. Of these, three clips were more than 3 cm from the lesion. Similarly, in 10 (20%) of 50 cases in which biopsy was performed with lateral compression, the clip was more than 1 cm from the lesion; in seven (14%) cases, the clip was more than 2 cm away on the postbiopsy craniocaudal projection.

Surgical excision was recommended for the treatment of 39 lesions diagnosed as atypical hyperplasia, ductal carcinoma in situ, or infiltrating carcinoma. Surgery was subsequently performed at our institution in 35 cases. The remaining four cases were lost to follow-up because the patients either returned or were referred to another facility for their definitive surgery. Of the 35 operations performed at our institution, preoperative wire local-

ization was performed in 30. Five of the 35 operations were mastectomies.

The metallic clip was used as the target for wire localization if the clip was within 1 cm of the original lesion on both projections. If there was a clip placement error of more than 1 cm on at least one projection, appropriate adjustment was made on the basis of the radiologist's evaluation of the pre- and postbiopsy mammograms (Fig 4). All adjustments made at preoperative needle localization were clearly communicated to the surgeon. The radiograph specimen with pathologic analysis confirmed excision of the clip and the residual lesion or the biopsy site in all cases.

Of the 39 lesions requiring definitive breast cancer surgery, 25 (64%) were retrospectively not visible on the mammograms obtained after percutaneous biopsy. However, 16 of these lesions were visible on subsequent surgical specimen radiographs. Histopathologic analysis of the remaining nine lesions verified excision of the biopsy cavity and/or residual lesion.

In five (13%) of the 39 lesions, the marker clip was more than 2 cm from the original lesion on at least one projection. Of these, three were malignant, and residual tumor was identified positively at histopathologic analysis of the surgical specimen. One of the five cases was lost to follow-up. One case of atypical ductal hyperplasia demonstrated no residual disease at surgical excision. The gross surgical specimen of this case measured 6.4 × 4.7 × 2.7 cm; a 0.4-cm hemorrhagic area, which indicated the previous biopsy site, was identified. Mammographic follow-up demonstrated stability of this case during the 2 years since biopsy.

In four (10%) of the 39 lesions requiring surgery, ductal carcinoma in situ and infiltrating breast carcinoma were later documented at surgery for two atypical ductal hyperplasia lesions and two ductal carcinoma in situ lesions that were diagnosed at stereotactic vacuum-assisted biopsy.

DISCUSSION

In our study, marker clip deployment was included in nearly half (111 [43%] of 258) of all stereotactic vacuum-assisted biopsies performed during the study period. The majority of these cases (72 [65%] of 111) were proved to be benign at histopathologic analysis. In retrospect, 28 (25%) of 111 lesions and 14 (19%) of 72 benign lesions were partially visible on the postbiopsy mammograms and theoretically may not have required a marker clip. The stereotactic images obtained after biopsy, however, were often limited due to their small field of view, poor compression, overlapping shadow of the biopsy probe, and obscuring hematoma. Because the decision whether to deploy a clip was based on the assessment of stereotactic images, we found that many clips were placed when the lesions were not visibly excised. Thus, careful attention to digital image optimization is one possible way to reduce unnecessary clip deployment.

Although a substantial number of cases requiring additional surgery demonstrated discrepancies between the location of the clip and the biopsy site, needle localization and excision were performed successfully. We believe that this success was likely related to our routine evaluation of the postbiopsy images and the prospective identification of inaccurate clip placement. Appropriate compensation was made during needle localization, which allowed successful surgical excision of all 30 surgical lesions in our series. In 15 (50%) of those 30 lesions, the clip was 1 cm or more from the biopsy site on at least one projection.

In our study, in all cases in which the clip was more than 2 cm away from the biopsy site, the discrepancy was evident in the plane orthogonal to the compression plane used for biopsy (z axis). Therefore, the importance of obtaining routine orthogonal-view screen-film mammograms after biopsy is twofold.

First, the final position of the marker clip is more accurately evaluated on screen-film mammograms than on stereotactic images. If there is an error in clip placement on one or both projections, the clip position and the distance away from the biopsy site can be clearly documented in the procedure report to ensure successful needle localization if definitive breast surgery is required. This documentation is particularly important if needle localization is performed at another institution or by another radiologist who is not familiar with the case. It is also important in cases in which the lesion is excised at stereotactic biopsy and residual hematoma and/or air is no longer identifiable at the time of needle localization.

Second, knowledge of the location of the clip in relation to the biopsy site on a two-view mammogram would aid in planning needle localization, since localization is most often performed with mammographic guidance. Because clip placement is most accurate in the plane used for percutaneous biopsy, we recommend performing needle localization in the same compression plane used for stereotactic biopsy to minimize sampling error at surgery. If there is substantial clip displacement, depth compensation can then be made in the orthogonal plane. Alternatively, Brenner (8) recently suggested that preoperative localization of excised lesion with the freehand technique, in which mammographic landmarks are used, may be a feasible option when there is a clip placement error. However, this type of localization requires sufficient experience with the freehand technique to ensure accuracy.

Previous study findings (4–6) on metallic clip placement during 11-gauge stereotactic core-needle biopsy, like ours, suggest that these clips provide an accurate and reliable method for marking the biopsy site when the mammographic lesion is no longer visible after biopsy. They also confirm that the metallic clip can be used as an accurate target when subsequent preoperative needle localization and surgical excision are indicated. However, several differences between our study and the previously published ones deserve comment.

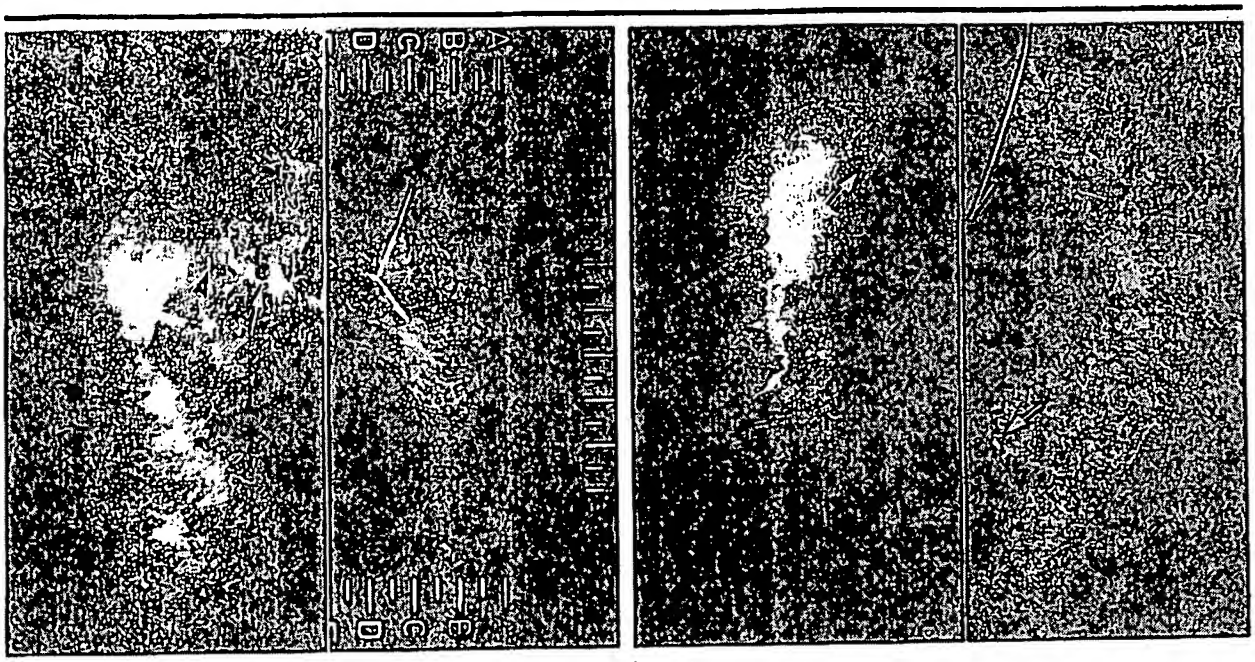
Both Liberman et al (4) and Reynolds (5) evaluated the accuracy of clip localization after stereotactic vacuum-assisted breast biopsy by comparing target and

TABLE 1
Accuracy of Clip Deployment at Breast Biopsy Performed with Craniocaudal Compression

Distance of Clip from Biopsy Site (mm)	No. of Clips (N = 61)	
	Craniocaudal Projection	Mediolateral Oblique Projection
≤5	53	43
6–10	7	5
11–19	1	5
>20	0	8

TABLE 2
Accuracy of Clip Deployment at Breast Biopsy Performed with Lateral Compression

Distance of Clip from Biopsy Site (mm)	No. of Clips (N = 50)	
	Craniocaudal Projection	Mediolateral Oblique Projection
≤5	24	41
6–10	9	6
11–19	10	3
>20	7	0



a. b.

Figure 4. Presurgical needle localization adjusted for clip placement error. A 49-year-old woman had a cluster of pleomorphic microcalcifications in the right posterior breast at the 10-o'clock position. The patient subsequently underwent stereotactic vacuum-assisted core-needle biopsy with lateral compression. All calcifications were removed, and a metallic clip was deployed to mark the biopsy site. Pathologic analysis revealed atypical lobular hyperplasia. (a) Left: Mediolateral mammogram obtained immediately after stereotactic biopsy demonstrates an air-containing cavity (arrow) at the biopsy site. The clip (arrowhead) is displaced approximately 10 mm from the site. Subsequent needle localization was also performed with a lateral approach. By using parenchymal landmarks, the original biopsy site was targeted. Right: Needle localization lateromedial projection obtained on an alphanumeric grid confirmed that the localizing wire is close to the original biopsy site. (b) Left: Prebiopsy craniocaudal mammogram demonstrates the original cluster of pleomorphic microcalcifications (arrow) in the posterior lateral right breast. Right: Corresponding needle-localization craniocaudal view is a mirror image of the mammogram. The metallic clip (arrow) is displaced approximately 7 cm medial to the biopsy site. By using parenchymal landmarks, successful needle localization of the original biopsy site was performed by compensating for depth error in this plane. Surgical histopathologic analysis yielded atypical lobular hyperplasia without evidence of carcinoma.

clip coordinates obtained from stereoradiographs. On the other hand, we relied on the measurement of clip-to-target and/or clip-to–biopsy site distances on dedicated screen-film mammograms obtained immediately after the biopsy. Although Liberman et al and Reynolds reported a much smaller percentage of cases with a clip-to-lesion distance greater than 1 cm compared with ours, the discrepancy is likely due to the different methods used to assess clip placement.

In fact, in our study there were only four (4%) of 111 cases that demonstrated clip-to-target distances greater than 1 cm in a plane other than the z axis. Liberman et al (4) and Reynolds (5) compared the stereo coordinates of the clip with the coordinates of the targeted lesion. The advantages of this technique are that it is quick, it is easily reproducible, and it provides measurements in the x, y, and z axes. The limitation, of course, is that these measurements are obtained while the breast is compressed, and small discrepancies, particularly in the z axis, may translate into larger distances because of the so-called accordion effect when the compression is released (4–6). Thus, even if the coordinates of the clip are close to the target and/or the biopsy site, a larger distance may be observed in an orthogonal plane postbiopsy mammogram. Although in both studies they commented on this phenomenon and recommended the acquisition of postbiopsy dedicated screen-film mammograms to avoid underestimation of the true distance between the biopsy site and the clip, they did not report these distances. We relied on direct measurement of the clip to the biopsy site, as demonstrated on the postbiopsy mammograms, so that displacement in the z axis was not underestimated.

Burbank and Forcier (6) used a mask measurement system to evaluate the location of the clip relative to the lesion examined at biopsy on dedicated screen-film mammograms. Their mask measurement system involved the creation of a mask by drawing localizing markers and the targeted lesion on the prebiopsy images in both projections onto clear films. The mask was then superimposed onto the postbiopsy image, and the position of the clip was drawn on the mask. Masks were created in both projections, which resulted in two masks per lesion undergoing biopsy. They then measured the distance from the clip to the center of the lesion on both masks and calculated the mean to determine the mean distance off target. Realizing that there would be some variability due to differences in technique, the authors also developed a calibration system based on mammograms of control benign lesions. Thus, they calculated the true distance between the clip and the lesion as the mean distance off target minus this correction factor. This mean, however, results in underestimation of the maximum clip-to–biopsy site displacement.

Although in both their study and ours

postbiopsy mammograms were used to measure the distance between the clip and the lesion, we did not use the mask measurement system. Instead, we chose a direct method of measurement when the biopsy site or residual lesion was visible. We used superimposed images when this was not possible. We then measured the distance from the center of the lesion and/or biopsy cavity to the clip in both obliquities instead of the mean of the distances. Therefore, we have a higher percentage (14% [15 of 111 clips] vs 7%) of clips placed by using the through probe technique that are greater than 2 cm from the biopsy site.

Our data reflect the maximum distance in either projection, not an average. We used this system for several reasons. The most important reason is that the true discrepancy between the clip and the biopsy location almost always occurs in the z axis. Therefore, a large z-axis discrepancy may be underestimated if it is averaged in the same case where there is small or no x- or y-axis discrepancy. In our study, all cases in which there was a large (>2-cm) discrepancy in the location of the clip versus the biopsy site, the displacement occurred in the plane perpendicular to the biopsy compression plane (z axis). In our study, we used a measurement system that reflected clinical practice and that closely illustrated the maximum clip displacement when present.

When the differences in the design of three studies are taken into account, the results are actually comparable. In our study, 75% of the lesions examined at biopsy performed with an 11-gauge mechanical cutter were not visible on postbiopsy mammograms. This finding is similar to the 72% of excisional biopsies reported by Burbank and Forcier (6). Liberman et al (4) reported that 71% were completely excised, although she reported an additional 10% that could not be evaluated due to obscuration from hematoma. In addition, our study findings demonstrated 15 (14%) of 111 lesions in which the location of the clip relative to the target was greater than 2 cm in one direction and eight (7%) that were greater or equal to 2.5 cm. This finding compares favorably with the 7% in Burbank's study in which the mean distance off target was greater than 24 mm. All study findings demonstrated a high degree of accuracy for clip placement in the x- and y-axes.

In conclusion, our study findings demonstrate that the location of the metallic clips deployed during stereotactic vacuum-assisted breast biopsy may differ substantially from the actual biopsy site, as demonstrated on dedicated postbiopsy screen-film mammograms. This discrepancy is typically in the plane perpendicular to that used for compression during biopsy (z axis) and is most likely due to the accordion effect (4). Although these clips are useful for marking a biopsy site when the visible portion of the lesion has been removed, careful correlation between the biopsy site and clip locations on two orthogonal mammographic images should be routinely performed after biopsy. These images will depict any discrepancies and allow accurate needle localization if it is subsequently required.

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